01

8/468145

Welcome to STN International! Enter x:x

LOGINID:ssspta1813nxm

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2	Jan 25	BLAST(R) searching in REGISTRY available in STN on the Web
NEWS	3	Jan 29	FSTA has been reloaded and moves to weekly updates
NEWS	4	Feb 01	DKILIT now produced by FIZ Karlsruhe and has a new update frequency
NEWS	5	Feb 19	Access via Tymnet and SprintNet Eliminated Effective 3/31/02
NEWS	6	Mar 08	Gene Names now available in BIOSIS
NEWS	7	Mar 22	TOXLIT no longer available
NEWS	8	Mar 22	TRCTHERMO no longer available
NEWS	9	Mar 28	US Provisional Priorities searched with P in CA/CAplus and USPATFULL
NEWS	10	Mar 28	LIPINSKI/CALC added for property searching in REGISTRY
NEWS	11	Apr 02	PAPERCHEM no longer available on STN. Use PAPERCHEM2 instead.
NEWS	12	Apr 08	"Ask CAS" for self-help around the clock
NEWS	13	Apr 09	BEILSTEIN: Reload and Implementation of a New Subject Area
NEWS	14	Apr 09	ZDB will be removed from STN
NEWS	15	Apr 19	US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
NEWS	16	Apr 22	Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS	17	Apr 22	BIOSIS Gene Names now available in TOXCENTER
NEWS	18	Apr 22	Federal Research in Progress (FEDRIP) now available
NEWS	19	Jun 03	New e-mail delivery for search results now available
NEWS	20	Jun 10	MEDLINE Reload
NEWS	21	Jun 10	PCTFULL has been reloaded
NEWS	22	Jul 02	FOREGE no longer contains STANDARDS file segment

NEWS EXPRESS	February 1 CURRENT WINDOWS VERSION IS V6.0d, CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP), AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

* * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 10:19:36 ON 03 JUL 2002

```
=> file biosis medline agricola embase caba wpids  japio biotechds lifesci caplus
uspatall
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.21       0.21

FILE 'BIOSIS' ENTERED AT 10:19:54 ON 03 JUL 2002
COPYRIGHT (C) 2002 BIOLOGICAL ABSTRACTS INC.(R)

FILE 'MEDLINE' ENTERED AT 10:19:54 ON 03 JUL 2002

FILE 'AGRICOLA' ENTERED AT 10:19:54 ON 03 JUL 2002

FILE 'EMBASE' ENTERED AT 10:19:54 ON 03 JUL 2002
COPYRIGHT (C) 2002 Elsevier Science B.V.  All rights reserved.

FILE 'CABA' ENTERED AT 10:19:54 ON 03 JUL 2002
COPYRIGHT (C) 2002 CAB INTERNATIONAL (CABI)

FILE 'WPIDS' ENTERED AT 10:19:54 ON 03 JUL 2002
COPYRIGHT (C) 2002 THOMSON DERWENT

FILE 'JAPIO' ENTERED AT 10:19:54 ON 03 JUL 2002
COPYRIGHT (C) 2002 Japanese Patent Office (JPO)

FILE 'BIOTECHDS' ENTERED AT 10:19:54 ON 03 JUL 2002
COPYRIGHT (C) 2002 THOMSON DERWENT AND INSTITUTE FOR SCIENTIFIC INFORMATION

FILE 'LIFESCI' ENTERED AT 10:19:54 ON 03 JUL 2002
COPYRIGHT (C) 2002 Cambridge Scientific Abstracts (CSA)


FILE 'CAPLUS' ENTERED AT 10:19:54 ON 03 JUL 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPATFULL' ENTERED AT 10:19:54 ON 03 JUL 2002
CA INDEXING COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPAT2' ENTERED AT 10:19:54 ON 03 JUL 2002
CA INDEXING COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

=> e engel jurgen/au
E1            1     ENGEL JULIE S/AU
E2            2     ENGEL JUNE/AU
E3          237 --> ENGEL JURGEN/AU
E4            1     ENGEL JURGN/AU
E5           22     ENGEL JUTTA/AU
E6          485     ENGEL K/AU
E7           12     ENGEL K A/AU
E8           21     ENGEL K C/AU
E9            1     ENGEL K D/AU
E10           6     ENGEL K E/AU
E11           2     ENGEL K G/AU
E12         173     ENGEL K H/AU

=> s e3
L1          237 "ENGEL JURGEN"/AU

=> e engel j/au
E1           24     ENGEL ISAAC/AU
```

```
E2            5     ENGEL IZO/AU
E3         2211 --> ENGEL J/AU
E4            4     ENGEL J */AU
E5          341     ENGEL J A/AU
E6            2     ENGEL J A B/AU
E7            4     ENGEL J A M/AU
E8            6     ENGEL J B/AU
E9            1     ENGEL J B VAN DE/AU
E10           5     ENGEL J B VAN DEN/AU
E11         274     ENGEL J C/AU
E12         460     ENGEL J D/AU

=> s e3
L2         2211 "ENGEL J"/AU

=> e wichert burkhard/au
E1            1     WICHERT BODO/AU
E2            9     WICHERT BRIGITTA/AU
E3           12 --> WICHERT BURKHARD/AU
E4            1     WICHERT BURKHARD V/AU
E5            5     WICHERT C/AU
E6            9     WICHERT D/AU
E7            1     WICHERT D M/AU
E8            7     WICHERT E/AU
E9            2     WICHERT E V O N/AU
E10           8     WICHERT EDWARD/AU
E11           1     WICHERT ERNEST J/AU
E12           5     WICHERT F/AU

=> s e3-e4
L3           13 ("WICHERT BURKHARD"/AU OR "WICHERT BURKHARD V"/AU)

=> e wichert b/au

E1           10     WICHERT ANA LAURO/AU
E2            4     WICHERT ANKE/AU
E3           46 --> WICHERT B/AU
E4            2     WICHERT B M/AU
E5            3     WICHERT B V/AU
E6            1     WICHERT BENNO/AU
E7            3     WICHERT BERND/AU
E8            1     WICHERT BERNHARD/AU
E9            1     WICHERT BIRGIT M/AU
E10           1     WICHERT BOB/AU
E11           1     WICHERT BODO/AU
E12           9     WICHERT BRIGITTA/AU

=> s e3-e5
L4           49 ("WICHERT B"/AU OR "WICHERT B M"/AU OR "WICHERT B V"/AU)

=> e sauerbier dieter/au
E1           19     SAUERBIER D/AU
E2            1     SAUERBIER DIESTER/AU
E3           28 --> SAUERBIER DIETER/AU
E4            1     SAUERBIER E/AU
E5            1     SAUERBIER F/AU
E6            3     SAUERBIER G A/AU
E7           18     SAUERBIER H/AU
E8            4     SAUERBIER HEINZ/AU
E9            1     SAUERBIER HERBERT/AU
E10          76     SAUERBIER I/AU
E11          15     SAUERBIER INGRID/AU
```

```
E12          12     SAUERBIER J/AU

=> s e1-e3
L5           48 ("SAUERBIER D"/AU OR "SAUERBIER DIESTER"/AU OR "SAUERBIER DIETER
                "/AU)

=> e reissmann thomas/au
E1            2     REISSMANN T L/AU
E2            8     REISSMANN TH/AU
E3           49 --> REISSMANN THOMAS/AU
E4            6     REISSMANN THOMAS L/AU
E5            7     REISSMANN U/AU
E6            2     REISSMANN ULRICH/AU
E7            9     REISSMANN ULRIKE/AU
E8            1     REISSMANN VALERIE/AU
E9            2     REISSMANN W/AU
E10           1     REISSMANN WALTER/AU
E11           1     REISSMANN WILFRIED/AU
E12          12     REISSMANN Z/AU

=> s e1-e4
L6           65 ("REISSMANN T L"/AU OR "REISSMANN TH"/AU OR "REISSMANN THOMAS"/A
                U OR "REISSMANN THOMAS L"/AU)

=> e reissmann t/au
E1            3     REISSMANN SIGMUND/AU
E2            1     REISSMANN STEFFEN/AU
E3          105 --> REISSMANN T/AU
E4            2     REISSMANN T L/AU
E5            8     REISSMANN TH/AU
E6           49     REISSMANN THOMAS/AU
E7            6     REISSMANN THOMAS L/AU
E8            7     REISSMANN U/AU
E9            2     REISSMANN ULRICH/AU
E10           9     REISSMANN ULRIKE/AU
E11           1     REISSMANN VALERIE/AU
E12           2     REISSMANN W/AU

=> s e3
L7           105 "REISSMANN T"/AU

=> s l1-l7
L8          2624 (L1 OR L2 OR L3 OR L4 OR L5 OR L6 OR L7)

=>
=> s l8 and cetrorelix
L9           146 L8 AND CETRORELIX

=> dup rem l9
PROCESSING COMPLETED FOR L9
L10           66 DUP REM L9 (80 DUPLICATES REMOVED)

=> s l10 and steril?
L11           4 L10 AND STERIL?

=> d bib ab 1-4

L11  ANSWER 1 OF 4  BIOSIS  COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN   2001:436900  BIOSIS
DN   PREV200100436900
TI   GnRH agonists and antagonists stimulate recovery of fertility in
     irradiated LBNF1 rats.
```

AU Meistrich, Marvin L. (1); Wilson, Gene; Shuttlesworth, Gladis; Huhtaniemi, Ilpo; **Reissmann, Thomas**

CS (1) Department of Experimental Radiation Oncology-66, MD Anderson Cancer Center, 1515 Holcombe Blvd, Houston, TX, 77030: meistrich@mdanderson.org USA

SO Journal of Andrology, (September October, 2001) Vol. 22, No. 5, pp. 809-817. print.
ISSN: 0196-3635.

DT Article

LA English

SL English

AB The goal of this study was to determine whether both gonadotropin-releasing hormone (GnRH) agonists and antagonists could enhance fertility in rats given **sterilizing** doses of irradiation, to quantify the levels of fertility, and to measure their relative effectiveness in stimulating recovery of spermatogenesis. Irradiated rats were treated with either the GnRH agonist Lupron or the GnRH antagonist **Cetrorelix**, which have different mechanisms of action. The antagonist suppressed luteinizing hormone (LH), reducing intratesticular testosterone from 75 ng/g-testis to about 5 ng/g-testis, whereas the agonist reduced intratesticular testosterone only moderately to about 20 ng/g-testis, presumably by direct action on the Leydig cell since LH was elevated. These differences were reflected in Leydig cell morphology. When hormone treatment was started immediately after 3.7-Gy irradiation, fertility was normal at week 20 in the agonist-treated rats and was near normal in antagonist-treated rats, whereas irradiated-only rats were **sterile**. At week 22 in the GnRH antagonist-treated rats, testicular weights and sperm counts were maintained at greater than 80% of control values; in GnRH agonist-treated rats, they were slightly but significantly lower than in GnRH antagonist-treated rats, and in irradiated-only rats, they were very low. When the treatment was initiated 10 weeks after 5-Gy irradiation, after spermatogenesis had ceased, fertility was restored at week 30 to subnormal levels in 83% of GnRH agonist- and 50% of GnRH antagonist-treated rats. Testis weights and sperm counts were restored to about 50% and 20% of control levels, respectively. The percentages of tubules with differentiated germ cells were higher in all groups of antagonist-treated rats than in those of agonist-treated rats. Thus, both GnRH agonists and antagonists produced dramatic recovery of spermatogenesis and fertility in irradiated rats, although there were differences in mechanism and perhaps also in effectiveness.

L11 ANSWER 2 OF 4 WPIDS (C) 2002 THOMSON DERWENT

AN 1999-542841 [46] WPIDS

CR 1994-265229 [33]

DNC C1999-158621

TI Treatment of female infertility, especially by in-vitro fertilization.

DC B04

IN **ENGEL, J; REISSMANN, T; SAUERBIER, D; WICHERT, B**

PA (ASTA) ASTA MEDICA AG

CYC 17

PI EP 947200 A2 19991006 (199946)* DE 5p
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE

ADT EP 947200 A2 Div ex EP 1994-101672 19940204, EP 1999-102340 19940204

FDT EP 947200 A2 Div ex EP 611572

PRAI DE 1993-4305225 19930219

AB EP 947200 A UPAB: 19991110
NOVELTY - **Sterile** freeze-dried **cetrorelix** acetate (a peptide described in EP299402) is used in the treatment of female infertility.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) use of **sterile** freeze-dried **cetrorelix**

acetate for protecting gonads against noxious agents that damage germ cells, e.g. radiation treatment and chemotherapy; (2) a composition comprising **sterile** freeze-dried **cetrorelix** acetate and optionally excipients for use in the treatment of female infertility; (3) a composition comprising **sterile** freeze-dried **cetrorelix** acetate and optionally excipients for protecting gonads against noxious agents that damage germ cells, e.g. radiation treatment and chemotherapy with cytostatic agents.

ACTIVITY - None given.

MECHANISM OF ACTION - Luteinizing hormone-releasing hormone (LHRH) antagonist.

USE - In an in-vitro fertilization procedure in which **cetrorelix** is administered to control the time of ovulation during an ovary stimulation treatment by preventing a pre-ovulation increase in luteinizing hormone (LH) levels, whereupon exogenous gonadotropin is administered to induce ovulation after follicle maturation.

Dwg.0/0

L11 ANSWER 3 OF 4 WPIDS (C) 2002 THOMSON DERWENT
AN 1994-265229 [33] WPIDS
DNC C1994-121294
TI Freeze-dried peptide compsns. - prepd. by freeze drying soln. of peptide in aq. acetic acid.
DC B04
IN **ENGEL, J; REISSMANN, T; SAUERBIER, D; WICHERT, B;** BURKHARD, W; JUERGEN, E
PA (ASTA) ASTA MEDICA AG
CYC 32
PI EP 611572 A2 19940824 (199433)* DE 5p
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
DE 4305225 A1 19940825 (199433) 5p
AU 9455235 A 19940825 (199436)
NO 9400564 A 19940822 (199436)
CA 2115943 A 19940820 (199439)
CZ 9400312 A3 19940914 (199439)
BR 9400617 A 19940927 (199440)
SK 9400195 A3 19940907 (199440)
FI 9400779 A 19940820 (199441)
JP 06271476 A 19940927 (199443) 5p
ZA 9401136 A 19941026 (199444) 12p
HU 67117 T 19950228 (199514)
EP 611572 A3 19950111 (199538)
AU 671881 B 19960912 (199644)
CN 1112019 A 19951122 (199737)
SG 46632 A1 19980220 (199822)
BR 1101004 A3 19980512 (199828)
CZ 284314 B6 19981014 (199847)
NZ 314707 A 19990225 (199914)
CZ 285768 B6 19991117 (200002)
EP 611572 B1 20000607 (200032) DE
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
DE 59409389 G 20000713 (200037)
HU 218281 B 20000728 (200045)
RU 2145234 C1 20000210 (200048)
ES 2148247 T3 20001016 (200058)
TW 387812 A 20000421 (200061)
ADT EP 611572 A2 EP 1994-101672 19940204; DE 4305225 A1 DE 1993-4305225 19930219; AU 9455235 A AU 1994-55235 19940217; NO 9400564 A NO 1994-564 19940218; CA 2115943 A CA 1994-2115943 19940218; CZ 9400312 A3 CZ 1994-312 19940214; BR 9400617 A BR 1994-617 19940218; SK 9400195 A3 SK 1994-195 19940218; FI 9400779 A FI 1994-779 19940218; JP 06271476 A JP 1994-20532 19940217; ZA 9401136 A ZA 1994-1136 19940218; HU 67117 T HU 1994-481

19940218; EP 611572 A3 EP 1994-101672 19940204; AU 671881 B AU 1994-55235 19940217; CN 1112019 A CN 1994-101378 19940218; SG 46632 A1 SG 1996-6874 19940204; BR 1101004 A3 BR 1997-1101004 19970514; CZ 284314 B6 CZ 1994-312 19940214; NZ 314707 A Div ex NZ 1994-250906 19940217, NZ 1994-314707 19940217; CZ 285768 B6 CZ 1998-974 19940214; EP 611572 B1 EP 1994-101672 19940204, Related to EP 1999-102340 19940204; DE 59409389 G DE 1994-509389 19940204, EP 1994-101672 19940204; HU 218281 B HU 1994-481 19940218; RU 2145234 C1 RU 1994-5001 19940218; ES 2148247 T3 EP 1994-101672 19940204; TW 387812 A TW 1994-100769 19940131

FDT AU 671881 B Previous Publ. AU 9455235; CZ 284314 B6 Previous Publ. CZ 9400312; NZ 314707 A Div ex NZ 250906; CZ 285768 B6 Previous Publ. CZ 9800974; EP 611572 B1 Related to EP 947200; DE 59409389 G Based on EP 611572; HU 218281 B Previous Publ. HU 67117; ES 2148247 T3 Based on EP 611572

PRAI DE 1993-4305225 19930219

AB EP 611572 A UPAB: 19991110

Freeze-dried compsns. comprising a peptide of 3-15 amino acid units and opt. one or more matrix materials are characterised in that 1 pt. wt. of the peptide is dissolved in 100-10,000 pts. wt. of acetic acid and then transferred to water and the resulting soln. is freeze dried.

USE/ADVANTAGE - The compsns. esp. contain **cetrorelix** (EP 299402), which is used in the treatment of female infertility (for controlling ovulation prior to isolating egg cells for in-vitro fertilisation) and for gonad protection in male patients (e.g. undergoing ratio- or chemotherapy). The aq. acetic acid soln. can be **sterilised** by filtration without gelation or hydrolysis of the peptide.

Dwg.0/0

L11 ANSWER 4 OF 4 USPATFULL

AN 2001:208180 USPATFULL

TI Method for the treatment of fertility disorders

IN **Engel, Jurgen**, Alzenau, Germany, Federal Republic of
Riethmuller-Winzen, Hilde, Frankfurt, Germany, Federal Republic of
Reissmann, Thomas, Frankfurt, Germany, Federal Republic of

PA Zentaris AG, Frankfurt am Main, Germany, Federal Republic of (non-U.S. corporation)

PI US 6319192 B1 20011120

AI US 1999-296610 19990423 (9)

PRAI US 1998-82743P 19980423 (60)

DT Utility

FS GRANTED

EXNAM Primary Examiner: Lacyk, John P.; Assistant Examiner: Cadugan, Joseph A

LREP Pillsbury Winthrop LLP

CLMN Number of Claims: 6

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 123

AB An improvement to the method of intrauterine insemination by the administration of luteinizing hormone-releasing hormone antagonists (LHRH antagonists).

=> d clm 4

L11 ANSWER 4 OF 4 USPATFULL

CLM What is claimed is:

1. In the method of therapeutic management of infertility by intrauterine insemination, the improvement consisting of a) the dose-dependent suppression of endogenous gonadotropins, especially LH, with an LH-RH antagonist allowing the maintenance of physiological oestrogen levels b) exogenous stimulation of the ovarian follicle growth

c) ovulation induction with HCG, native LHRH, LHRH agonists or recombinant LH d) intrauterine insemination by sperm injection.

2. The method of therapeutic management of infertility by intrauterine insemination according to claim 1 in which the LHRH antagonist is **cetrorelix.**

3. The method of therapeutic management of infertility by intrauterine insemination according to claim 1 in which he LHRH antagonist is antarelix.

4. The method of therapeutic management of infertility by intrauterine insemination according to claim 1 in which ovarian follicle stimulation is performed by administration of urinary or recombinant FSH or HMG, with or without recombinant LH.

5. The method of therapeutic management of infertility by intrauterine insemination according to claim 1 in which ovarian follicle stimulation is achieved with antioestrogens.

6. The method of therapeutic management of infertility by intrauterine insemination according to claim 1 in which ovarian follicle stimulation is achieved with the combination of antioestrogens with gonadotropins.

```
=> d his

     (FILE 'HOME' ENTERED AT 10:19:36 ON 03 JUL 2002)

     FILE 'BIOSIS, MEDLINE, AGRICOLA, EMBASE, CABA, WPIDS, JAPIO, BIOTECHDS,
     LIFESCI, CAPLUS, USPATFULL, USPAT2' ENTERED AT 10:19:54 ON 03 JUL 2002
                 E ENGEL JURGEN/AU
L1           237 S E3
                 E ENGEL J/AU
L2          2211 S E3
                 E WICHERT BURKHARD/AU
L3            13 S E3-E4
                 E WICHERT B/AU
L4            49 S E3-E5
                 E SAUERBIER DIETER/AU
L5            48 S E1-E3
                 E REISSMANN THOMAS/AU
L6            65 S E1-E4
                 E REISSMANN T/AU
L7           105 S E3
L8          2624 S L1-L7
L9           146 S L8 AND CETRORELIX
L10           66 DUP REM L9 (80 DUPLICATES REMOVED)
L11            4 S L10 AND STERIL?

=> s l10 and lyophil?
L12            4 L10 AND LYOPHIL?

=> d bib 1-4

L12  ANSWER 1 OF 4  BIOSIS  COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN   2000:477618  BIOSIS
DN   PREV200000477618
TI   Process for the preparation of immobilized and activity-stabilized
     complexes of LHRH antagonists.
AU   Engel, Jurgen (1); Deger, Wolfgang; Reissmann, Thomas;
```

Losse, Gunter; Naumann, Wolfgang; Murgas, Sandra
CS (1) Alzenau Germany
ASSIGNEE: Asta Medica Aktiengesellschaft, Dresden, Germany
PI US 6054555 April 25, 2000
SO Official Gazette of the United States Patent and Trademark Office Patents, (Apr. 25, 2000) Vol. 1233, No. 4, pp. No pagination. e-file. ISSN: 0098-1133.
DT Patent
LA English

L12 ANSWER 2 OF 4 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:355483 BIOSIS
DN PREV200000355483
TI Immobilized and activity-stabilized complexes of LHRH antagonists and processes for their preparation.
AU **Engel, Jurgen (1)**; Deger, Wolfgang; **Reissmann, Thomas**; Losse, Gunter; Naumann, Wolfgang; Murgas, Sandr
CS (1) Alzenau Germany
ASSIGNEE: Asta Medica Aktiengesellschaft, Dresden, Germany
PI US 6022860 February 08, 2000
SO Official Gazette of the United States Patent and Trademark Office Patents, (Feb. 8, 2000) Vol. 1231, No. 2, pp. No pagination. e-file. ISSN: 0098-1133.
DT Patent
LA English

L12 ANSWER 3 OF 4 WPIDS (C) 2002 THOMSON DERWENT
AN 2002-257593 [30] WPIDS
DNC C2002-076695
TI Basic peptide acid addition salt preparation, for use in parenteral medicaments, comprises reacting starting salt with mixed bed ion exchanger followed by acid.
DC B04
IN BAUER, H; DAMM, M; **ENGEL, J**; SOLONEK, W; STACH, G; SALONEK, W
PA (ASTA) ASTA MEDICA AG; (ZENT-N) ZENTARIS AG
CYC 56
PI WO 2002014347 A2 20020221 (200230)* DE
RW: AT BE CH CY DE DK EA ES FI FR GB GR IE IT LU MC NL PT SE TR
W: AU BG BR BY CA CN CO CZ EE GE HR HU ID IL IN IS JP KG KR KZ LT LV MK MX NO NZ PL RO RU SG SI SK TR UA UZ YU ZA
DE 10040700 A1 20020228 (200230)
ADT WO 2002014347 A2 WO 2001-EP9219 20010809; DE 10040700 A1 DE 2000-10040700 20000817
PRAI DE 2000-10040700 20000817

L12 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2002 ACS
AN 1998:672495 CAPLUS
DN 129:293891
TI Immobilized activity-stabilized LHRH antagonist complexes and their production
IN Engel, Juergen; Deger, Wolfgang; **Reissmann, Thomas**; Losse, Guenter; Naumann, Wolfgang; Murgas, Sandra
PA Asta Medica Aktiengesellschaft, Germany
SO PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9842381	A1	19981001	WO 1998-EP1398	19980311
	W: AU, BR, CA, CN, CZ, HU, IL, JP, MX, NO, NZ, PL, RU, SK, TR, UA				

```
        RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
     DE 19712718       A1   19981001       DE 1997-19712718 19970326
     DE 19712718       C2   19990923
     AU 9869207        A1   19981020       AU 1998-69207    19980311
     BR 9807887        A    20000222       BR 1998-7887     19980311
     EP 981377         A1   20000301       EP 1998-914877   19980311
        R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, FI
     JP 2001520662     T2   20011030       JP 1998-544811   19980311
     US 6022860        A    20000208       US 1998-48244    19980326
     NO 9904665        A    19990924       NO 1999-4665     19990924
     US 6054555        A    20000425       US 1999-422990   19991022
PRAI DE 1997-19712718  A    19970326
     WO 1998-EP1398    W    19980311
     US 1998-48244     A3   19980326


=> s l10 and (prepar? or makin?)
   8 FILES SEARCHED...
L13          10 L10 AND (PREPAR? OR MAKIN?)

=> d bib ab 1-10

L13  ANSWER 1 OF 10  BIOSIS  COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN   2001:192045  BIOSIS
DN   PREV200100192045
TI   Diagnostic composition containing an LH-RH antagonist for hysteroscopy.
AU   Engel, Jurgen (1); Diedrich, Klaus; Felberbaum, Ricardo
CS   (1) Alzenau Germany
     ASSIGNEE: Asta Medica Aktiengesellschaft, Germany
PI   US 6106805 August 22, 2000
SO   Official Gazette of the United States Patent and Trademark Office Patents,
     (Aug. 22, 2000) Vol. 1237, No. 4, pp. No Pagination. e-file.
     ISSN: 0098-1133.
DT   Patent
LA   English
AB   The invention relates to a diagnostic composition for improving the
     effectiveness of hysteroscopy, characterized in that it contains an LH-RH
     antagonist, in particular cetrorelix. The composition is
     envisaged for use prior to hysteroscopy and/or for preparation
     for surgery, specifically in a single dose of between 0.1 and 2 mg/kg.
     However, the composition can also be administered, for use prior to
     hysteroscopy and/or for preparation for surgery, in a multiple
     dose of between 0.01 and 0.5 mg/kg, preferably spread over 1-14 days. The
     composition is furthermore suitable for use in hysteroscopy in combination
     with the subsequent treatment of pathological conditions of the uterus
     such as myoma and endometrial hyperplasia.

L13  ANSWER 2 OF 10  BIOSIS  COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN   2000:477618  BIOSIS
DN   PREV200000477618
TI   Process for the preparation of immobilized and
     activity-stabilized complexes of LHRH antagonists.
AU   Engel, Jurgen (1); Deger, Wolfgang; Reissmann, Thomas;
     Losse, Gunter; Naumann, Wolfgang; Murgas, Sandra
CS   (1) Alzenau Germany
     ASSIGNEE: Asta Medica Aktiengesellschaft, Dresden, Germany
PI   US 6054555 April 25, 2000
SO   Official Gazette of the United States Patent and Trademark Office Patents,
     (Apr. 25, 2000) Vol. 1233, No. 4, pp. No pagination. e-file.
     ISSN: 0098-1133.
DT   Patent
```

LA English
AB In this invention, a release-delaying system is to be developed for LHRH antagonists, in particular for **cetrorelix**, which allows the active compound to be released in a controlled manner over several weeks by complexation with suitable biophilic carriers. The acidic polyamino acids polyglutamic acid and polyaspartic acid were selected for complexation with **cetrorelix**. The **cetrorelix** polyamino acid complexes are **prepared** from aqueous solutions by combination of the solutions and precipitation of the complexes, which are subsequently centrifuged off and dried over P2 O5 in vacuo. If complexes having a defined composition are to be obtained, lyophilization proves to be a suitable method. The **cetrorelix**-carboxylic acid complexes were also **prepared** from the aqueous solutions. In the random liberation system, the acidic polyamino acids poly-Glu and poly-Asp showed good release-delaying properties as a function of the hydrophobicity and the molecular mass of the polyamino acid. In animal experiments, it was possible to confirm the activity of the **cetrorelix**-polyamino acid complexes as a depot system in principle. It is thus possible by complexation of **cetrorelix** with polyamino acids to achieve testosterone suppression in male rats over 600 hours. The release of active compound here can be controlled by the nature and the molecular mass of the polymers.

L13 ANSWER 3 OF 10 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:355483 BIOSIS
DN PREV200000355483
TI Immobilized and activity-stabilized complexes of LHRH antagonists and processes for their **preparation**.
AU **Engel, Jurgen (1)**; Deger, Wolfgang; **Reissmann, Thomas**; Losse, Gunter; Naumann, Wolfgang; Murgas, Sandr
CS (1) Alzenau Germany
ASSIGNEE: Asta Medica Aktiengesellschaft, Dresden, Germany
PI US 6022860 February 08, 2000
SO Official Gazette of the United States Patent and Trademark Office Patents, (Feb. 8, 2000) Vol. 1231, No. 2, pp. No pagination. e-file. ISSN: 0098-1133.
DT Patent
LA English
AB In this invention, a release-delaying system is to be developed for LHRH antagonists, in particular for **cetrorelix**, which allows the active compound to be released in a controlled manner over several weeks by complexation with suitable biophilic carriers. The acidic polyamino acids polyglutamic acid and polyaspartic acid were selected for complexation with **cetrorelix**. The **cetrorelix** polyamino acid complexes are **prepared** from aqueous solutions by combination of the solutions and precipitation of the complexes, which are subsequently centrifuged off and dried over P2 O5 in vacuo. If complexes having a defined composition are to be obtained, lyophilization proves to be a suitable method. The **cetrorelix**-carboxylic acid complexes were also **prepared** from the aqueous solutions. In the random liberation system, the acidic polyamino acids poly-Glu and poly-Asp showed good release-delaying properties as a function of the hydrophobicity and the molecular mass of the polyamino acid. In animal experiments, it was possible to confirm the activity of the **cetrorelix**-polyamino acid complexes as a depot system in principle. It is thus possible by complexation of **cetrorelix** with polyamino acids to achieve testosterone suppression in male rats over 600 hours. The release of active compound here can be controlled by the nature and the molecular mass of the polymers.

L13 ANSWER 4 OF 10 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1998:354009 BIOSIS

DN PREV199800354009
TI Treatment of uterine fibroids with a slow-release formulation of the gonadotrophin releasing hormone antagonist **Cetrorelix**.
AU Felberbaum, R. E. (1); Germer, U.; Ludwig, M.; Riethmueller-Winzen, H.; Heise, S.; Buttge, I.; Bauer, O.; **Reissmann, T.**; **Engel, J.**; Diedrich, K.
CS (1) Dep. Obstet. Gynecol., Med. Univ. Luebeck, Ratzeburger Allee 160, 23538 Luebeck Germany
SO Human Reproduction (Oxford), (June, 1998) Vol. 13, No. 6, pp. 1660-1668. ISSN: 0268-1161.
DT Article
LA English
AB A depot **preparation** of the third-generation gonadotrophin-releasing hormone (GnRH) antagonist **Cetrorelix** (SB-75) was used for preoperative treatment in twenty premenopausal patients with symptomatic uterine fibroids who were to undergo surgery. In a prospective, open, randomized setting 60 mg of **Cetrorelix** pamoate salt was administered i.m. on cycle day 2. Patients were randomized for a second dose of 30 or 60 mg of **Cetrorelix** depot, which was administered according to the degree of oestradiol suppression (<50 pg/ml) on treatment day 21 or 28. Surgery was done after 6 or 8 weeks of treatment, depending on second dosage administration. Weekly transvaginal sonography (TVS) and magnetic resonance imaging (MRI) before and after treatment was performed, for fibroid volume assessment. Sixteen patients showed satisfactory suppression of gonadotrophins and sex steroid secretion, avoiding any initial flare-up effect. In these patients a mean shrinkage rate of largest fibroid volume of 33.5% at the end of treatment could be observed according to TVS, while the mean shrinkage rate obtained after 14 days of treatment was 31.3%. In good responders (shrinkage >20%) largest fibroid volume at day 14 was -56.7% of basic assessment. Although MRI showed minor mean shrinkage rates of only 25.4% of the initial volume, these differences in comparison to TVS assessment were not statistically significant. The avoidance of any initial flare-up in gonadotrophin secretion may explain this extremely fast reduction in fibroid size. The advantages of GnRH antagonist treatment in this indication consist in the short treatment time with a fast restoration of the ovarian function. The rate of poor responders may be reduced by using an improved slow release **preparation**.

L13 ANSWER 5 OF 10 WPIDS (C) 2002 THOMSON DERWENT
AN 2002-257593 [30] WPIDS
DNC C2002-076695
TI Basic peptide acid addition salt **preparation**, for use in parenteral medicaments, comprises reacting starting salt with mixed bed ion exchanger followed by acid.
DC B04
IN BAUER, H; DAMM, M; **ENGEL, J**; SOLONEK, W; STACH, G; SALONEK, W
PA (ASTA) ASTA MEDICA AG; (ZENT-N) ZENTARIS AG
CYC 56
PI WO 2002014347 A2 20020221 (200230)* DE
RW: AT BE CH CY DE DK EA ES FI FR GB GR IE IT LU MC NL PT SE TR
W: AU BG BR BY CA CN CO CZ EE GE HR HU ID IL IN IS JP KG KR KZ LT LV MK MX NO NZ PL RO RU SG SI SK TR UA UZ YU ZA
DE 10040700 A1 20020228 (200230)
ADT WO 2002014347 A2 WO 2001-EP9219 20010809; DE 10040700 A1 DE 2000-10040700 20000817
PRAI DE 2000-10040700 20000817
AB WO 200214347 A UPAB: 20020513
NOVELTY - **Preparation** of a peptide acid addition salt (I) comprises: (a) reacting a starting acid addition salt (II) of a basic peptide with a mixed bed ion exchanger (or a mixture of acidic and basic ion exchangers) in presence of a diluent; (b) reacting the obtained free

basic peptide with an inorganic or organic acid to give (I); and (c) removing the diluent.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for:

(i) (I) obtained by the process (specifically in lyophilized form);

(ii) a pharmaceutical **preparation** containing (I) obtained by the process, together with auxiliaries, carriers and/or structuring agents; and

(iii) the production of a **preparation** as in (ii), by adding the auxiliaries, carriers and/or structuring agents at least partially before removing the solvent.

USE - The use of (I) obtained by the process is claimed in the production of a medicament for parenteral administration to mammals. In particular the process is used for **preparing** sparingly soluble salts of LHRH agonists or antagonists (e.g. **cetrorelix** embonate) for providing prolonged action on parenteral administration. (I) are typically used for treating BPH, myoma or endometriosis.

Dwg.0/1

L13 ANSWER 6 OF 10 WPIDS (C) 2002 THOMSON DERWENT
AN 2001-006781 [01] WPIDS
DNC C2001-001469
TI Improvement to a method of therapeutic management of infertility by programming of controlled ovarian stimulation and assisted reproductive procedures.
DC B04
IN **ENGEL, J**; RITHMUELLER-WINZEN, H; RIETHMUELLER-WINZEN, H
PA (ASTA) ASTA MEDICA AG; (ZENT-N) ZENTARIS AG
CYC 56
PI WO 2000059542 A1 20001012 (200101)* EN 17p
RW: AT BE CH CY DE DK EA ES FI FR GB GR IE IT LU MC NL PT SE
W: AU BG BR BY CA CN CZ EE GE HR HU ID IL IN IS JP KG KR KZ LT LV MK MX NO NZ PL RO RU SG SI SK TR UA UZ YU ZA
AU 2000041069 A 20001023 (200107)
NO 2001004736 A 20011126 (200207)
BR 2000009477 A 20020108 (200208)
EP 1165138 A1 20020102 (200209) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
KR 2001105401 A 20011128 (200233)
ADT WO 2000059542 A1 WO 2000-EP2466 20000321; AU 2000041069 A AU 2000-41069 20000321; NO 2001004736 A WO 2000-EP2466 20000321, NO 2001-4736 20010928; BR 2000009477 A BR 2000-9477 20000321, WO 2000-EP2466 20000321; EP 1165138 A1 EP 2000-920521 20000321, WO 2000-EP2466 20000321; KR 2001105401 A KR 2001-712422 20010928
FDT AU 2000041069 A Based on WO 200059542; BR 2000009477 A Based on WO 200059542; EP 1165138 A1 Based on WO 200059542
PRAI US 1999-131632P 19990428; US 1999-127241P 19990331
AB WO 200059542 A UPAB: 20001230

NOVELTY - Improvement to a method of therapeutic management of infertility by programming of controlled ovarian stimulation (COS) and assisted reproductive procedures (ART), comprising suppression of premature ovulation, programming the start of COS, exogenous stimulation of ovarian follicle growth, ovulation induction and application of ART.

DETAILED DESCRIPTION - In the method of therapeutic management of infertility by programming of controlled ovarian stimulation (COS) and assisted reproductive procedures (ART) the improvement consisting of: (a) suppression of premature ovulation with an LHRH-antagonist in COS and ART with multiple follicle and oocytes development; (b) programming the start of COS by the administration of progestogen only - or alternatively combined oral contraceptive **preparations**; (c) exogenous stimulation of the ovarian follicle growth; (d) ovulation induction with HCG, native LHRH, LHRH-agonists or recombinant LH; and (e) application of

ART, especially IVF, ICSI, GIFT, ZIFT or by intrauterine insemination by sperm injection.

ACTIVITY - Contraceptive.

MECHANISM OF ACTION - LHRH-antagonist; LHRH-agonist.

USE - The method is used for the therapeutic management of infertility (claimed).

ADVANTAGE - The method allows for the start of a menstrual cycle and of COS to be programmed, thereby allowing oocytes pick up and fertilization procedures to be performed during Mondays to Fridays.
Dwg.0/0

L13 ANSWER 7 OF 10 WPIDS (C) 2002 THOMSON DERWENT
AN 1994-265229 [33] WPIDS
DNC C1994-121294
TI Freeze-dried peptide compsns. - prepd. by freeze drying soln. of peptide in aq. acetic acid.
DC B04
IN **ENGEL, J; REISSMANN, T; SAUERBIER, D; WICHERT, B;** BURKHARD, W; JUERGEN, E
PA (ASTA) ASTA MEDICA AG
CYC 32
PI EP 611572 A2 19940824 (199433)* DE 5p
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
DE 4305225 A1 19940825 (199433) 5p
AU 9455235 A 19940825 (199436)
NO 9400564 A 19940822 (199436)
CA 2115943 A 19940820 (199439)
CZ 9400312 A3 19940914 (199439)
BR 9400617 A 19940927 (199440)
SK 9400195 A3 19940907 (199440)
FI 9400779 A 19940820 (199441)
JP 06271476 A 19940927 (199443) 5p
ZA 9401136 A 19941026 (199444) 12p
HU 67117 T 19950228 (199514)
EP 611572 A3 19950111 (199538)
AU 671881 B 19960912 (199644)
CN 1112019 A 19951122 (199737)
SG 46632 A1 19980220 (199822)
BR 1101004 A3 19980512 (199828)
CZ 284314 B6 19981014 (199847)
NZ 314707 A 19990225 (199914)
CZ 285768 B6 19991117 (200002)
EP 611572 B1 20000607 (200032) DE
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
DE 59409389 G 20000713 (200037)
HU 218281 B 20000728 (200045)
RU 2145234 C1 20000210 (200048)
ES 2148247 T3 20001016 (200058)
TW 387812 A 20000421 (200061)
ADT EP 611572 A2 EP 1994-101672 19940204; DE 4305225 A1 DE 1993-4305225 19930219; AU 9455235 A AU 1994-55235 19940217; NO 9400564 A NO 1994-564 19940218; CA 2115943 A CA 1994-2115943 19940218; CZ 9400312 A3 CZ 1994-312 19940214; BR 9400617 A BR 1994-617 19940218; SK 9400195 A3 SK 1994-195 19940218; FI 9400779 A FI 1994-779 19940218; JP 06271476 A JP 1994-20532 19940217; ZA 9401136 A ZA 1994-1136 19940218; HU 67117 T HU 1994-481 19940218; EP 611572 A3 EP 1994-101672 19940204; AU 671881 B AU 1994-55235 19940217; CN 1112019 A CN 1994-101378 19940218; SG 46632 A1 SG 1996-6874 19940204; BR 1101004 A3 BR 1997-1101004 19970514; CZ 284314 B6 CZ 1994-312 19940214; NZ 314707 A Div ex NZ 1994-250906 19940217, NZ 1994-314707 19940217; CZ 285768 B6 CZ 1998-974 19940214; EP 611572 B1 EP 1994-101672 19940204, Related to EP 1999-102340 19940204; DE 59409389 G DE 1994-509389 19940204, EP 1994-101672 19940204; HU 218281 B HU 1994-481 19940218; RU

2145234 C1 RU 1994-5001 19940218; ES 2148247 T3 EP 1994-101672 19940204; TW 387812 A TW 1994-100769 19940131
FDT AU 671881 B Previous Publ. AU 9455235; CZ 284314 B6 Previous Publ. CZ 9400312; NZ 314707 A Div ex NZ 250906; CZ 285768 B6 Previous Publ. CZ 9800974; EP 611572 B1 Related to EP 947200; DE 59409389 G Based on EP 611572; HU 218281 B Previous Publ. HU 67117; ES 2148247 T3 Based on EP 611572
PRAI DE 1993-4305225 19930219
AB EP 611572 A UPAB: 19991110
Freeze-dried compsns. comprising a peptide of 3-15 amino acid units and opt. one or more matrix materials are characterised in that 1 pt. wt. of the peptide is dissolved in 100-10,000 pts. wt. of acetic acid and then transferred to water and the resulting soln. is freeze dried.
USE/ADVANTAGE - The compsns. esp. contain **cetrorelix** (EP 299402), which is used in the treatment of female infertility (for controlling ovulation prior to isolating egg cells for in-vitro fertilisation) and for gonad protection in male patients (e.g. undergoing ratio- or chemotherapy). The aq. acetic acid soln. can be sterilised by filtration without gelation or hydrolysis of the peptide.
Dwg.0/0

L13 ANSWER 8 OF 10 USPATFULL
AN 2000:70812 USPATFULL
TI Means for treating prostate hypertrophy and prostate cancer
IN **Engel, Jurgen**, Alzenau, Germany, Federal Republic of
Reissmann, Thomas, Frankfurt am Main, Germany, Federal Republic of
Riethmuller-Winzen, Hilde, Frankfurt am Main, Germany, Federal Republic of
Rawert, Jurgen, Alzenau, Germany, Federal Republic of
PA ASTA Medica AG, Dresden, Germany, Federal Republic of (non-U.S. corporation)
PI US 6071882 20000606
AI US 1998-62704 19980420 (9)
RLI Division of Ser. No. US 1997-908198, filed on 7 Aug 1997
PRAI US 1996-25990P 19960912 (60)
US 1997-43228P 19970410 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Goldberg, Jerome D.
LREP Pillsbury Madison & Sutro LLP
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN 4 Drawing Figure(s); 4 Drawing Page(s)
LN.CNT 273
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A regime for therapeutic management of a benign prostatic hyperplasia and prostatic cancer employs **Cetrorelix** alone or in combination with .alpha.-reductase inhibitors or .alpha.-receptor blocking agents. The regimen reduces the volume of the prostate and avoids the side effects associated with testosterone levels being in a castration range. **Cetrorelix** is administered at dosages between 0.5 mg/day and 20 mg/week or about 0.014 mg/kg body weight per day to 0.30 mg/kg body weight per week or at levels of about 25 to 120 mg of **Cetrorelix** per month or 0.376 mg/kg to 1.71 mg/kg per month. **Cetrorelix** can be administered with .alpha.-reductase inhibitors or .alpha.-receptor blocking agents.

L13 ANSWER 9 OF 10 USPATFULL
AN 1999:146533 USPATFULL
TI Nova- and decapeptides in the **preparation** of a drug for the treatment of aids

IN **Engel, Jurgen**, Alzenau, Germany, Federal Republic of
Kutscher, Bernhard, Maintal, Germany, Federal Republic of
Bernd, Michael, Frankfurt am Main, Germany, Federal Republic of
Niemeyer, Ulf, Offenbach, Germany, Federal Republic of
PA ASTA Medica AG, Germany, Federal Republic of (non-U.S. corporation)
PI US 5985834 19991116
WO 9500168 19950105
AI US 1995-569111 19951218 (8)
WO 1994-EP1037 19940402
19951218 PCT 371 date
19951218 PCT 102(e) date
PRAI DE 1993-4320201 19930618
DT Utility
FS Granted
EXNAM Primary Examiner: Tsang, Cecilla J.; Assistant Examiner: Delacroix-Muirheid, C.
LREP Cushman Darby & Cushman IP Group of Pillsbury Madison & Sutro LLP
CLMN Number of Claims: 24
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 424
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Described are LHRH-antagonistic and bombesin-antagonistic nona- and decapeptides suitable for use in the **preparation** of a drug for the treatment of AIDS and ARC as well as for use in the **preparation** of an immunostimulation drug.

L13 ANSWER 10 OF 10 USPATFULL
AN 95:43015 USPATFULL
TI Compressed gas packages using polyoxyethylene glyceryl oleates
IN Hettche, Helmut, Dietzenbach, Germany, Federal Republic of
Engel, Jurgen, Alzenau, Germany, Federal Republic of
Muckenschnabel, Reinhard, Frankfurt, Germany, Federal Republic of
PA Asta Medica Aktiengesellschaft, Dresden, Germany, Federal Republic of (non-U.S. corporation)
PI US 5415853 19950516
AI US 1993-33789 19930317 (8)
PRAI DE 1992-42085055 19920317
DE 1992-42151880 19920508
DE 1992-42308763 19920916
DT Utility
FS Granted
EXNAM Primary Examiner: Page, Thurman K.; Assistant Examiner: Benston, Jr., William E.
LREP Cushman Darby & Cushman
CLMN Number of Claims: 6
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 314
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Aerosol compressed gas packages containing a member of the group consisting of polyoxyethylene-25-glyceryl trioleate, polyoxyethylene-30-glyceryl monooleate and polyoxyethylene-20-glyceryl monooleate as suspension stabilizer and/or valve lubricant. These materials are especially useful when the package contains TG 227 or TG 134a as the propellant.

=> d clm 8-10

L13 ANSWER 8 OF 10 USPATFULL
CLM What is claimed is:

1. A regime for therapeutic management of benign prostatic hyperplasia in a mammalian organism without testosterone levels being in castration range comprising the administration of an effective synergistic amount of LH-RH antagonist **Cetrorelix** in combination with .alpha.-receptor blocking agents according to a regime wherein **Cetrorelix** is administered over time and in a dosage amount sufficient to reduce the volume of the prostrate, BPH symtoms and/or prostate specific antigen levels, without the side effects associated with testosterone levels being in a castration range.

2. The regime according to claim 1 which involves the administration of **Cetrorelix** at dosages between 0.5 mg/day and 20 mg/week or about 0.007 mg/kg body weight per day to 0.30 mg/kg body weight per week.

3. The regime according to claim 1 wherein the dosage amount is at levels of about 20 to 120 mg of **Cetrorelix** per month or about 0.285 mg/kg to 1.71 mg/kg per month for one to six months.

4. The treatment according to claim 1 or 3 wherein **Cetrorelix** is administered with .alpha.-receptor blocking agents in a specific timely regime.

5. The treatment according to claim 1 or 3 wherein the timely regime is as follows: 1 to 12 weeks of **Cetrorelix** treatment followed by 1 to 12 weeks of treatment with an .alpha.-receptor blocking agent.

6. The treatment according to claim 5 wherein the regime is as follows: 1 to 12 weeks of **Cetrorelix** treatment followed by 1-12 weeks treatment with an .alpha.-receptor blocking agent used for the treatment of BPH; or alternatively, 1-12 weeks of **Cetrorelix** treatment followed by continuous treatment with an .alpha.-receptor blocking agent and retreatment with **Cetrorelix** after six months.

7. The regime according to claim 1 comprising the administration of about 0.5 to 5 mg per day **Cetrorelix** for 1 to 12 weeks continuously or intermittently, together with an .alpha.-receptor blocking agent, optionally followed by retreatment with **Cetrorelix** alone or with an .alpha.-receptor blocking agent after 6 months.

8. The regime according to claim 1 wherein the .alpha.-receptor blocking agent is a uroselective .alpha.-1 adrenoceptor blocking agent.

9. The regime according to claim 8 wherein the uroselective .alpha.-1 adrenoceptor blocking agent is selected from the group consisting of Naftopidil, Terazosin, Doxazosin and Tamsulosin.

10. The regime according to claim 9 wherein the uroselective .alpha.-1 adrenoceptor blocking agent is administered in a daily dosage of 2 mg to 10 mg.

11. The regime according to claim 1 wherein the .alpha.-receptor blocking agent is Naftopidil.

12. The regime according to claim 3 wherein the dosage amount is at levels abour 20 to 120 mg **Cetrorelix** per month or about 0.285 mg/kg to 1.71 mg/kg per month for one to three months.

L13 ANSWER 9 OF 10 USPATFULL
CLM What is claimed is:
1. A method of combating a virus that causes a disease selected from the

group consisting of AIDS and AIDS related complex (ARC) by administering a pharmaceutically effective amount of at least one peptide with an amino acid sequence according to the general Formula I Ac-D-Nal(2)-D-Phe(4-Cl)-xxx-A-B-yyy-zzz-Arg-C-D-Ala-NH.sub.2 wherein

---

xxx =
D-Pal(3), [D-phe(4-Cl),] or D-Trp
yyy = D-Cit, D-Lys(R), [D-Arg] or D-Hci
R is selected from the group consisting of C.sub.1 -C.sub.4)-acyl and (C.sub.1 -C.sub.10-)-alkyl,
zzz = L-Leu, Nle, Nva, or t-Leu
A = Ser, Ser(sugar)
wherein sugar is selected from the group consisting of glucose, galactose, allose, altrose, manose, gulose, idose and talose.
B = Tyr, Lys(Nic), or Mop
C = Pro, or Ala

---

or a pharmaceutically acceptable salt thereof optionally inlcuding hydrochloride, trifluoroacetate, acetate, sulfate, phosphate, mesylate or tosylate.

2. The method of claim 1, wherein said pharmaceutically effective amount of said at least one peptide is effective to protect T-lymphocytes infected with said virus.

3. The method of claim 1, wherein said pharmaceutically effective amount of said at least one peptide is effective to combat said virus by inhibiting proliferation of said virus.

4. A method of combating a virus that causes a disease selected from the group consisting of AIDS and ARC by administering a pharmaceutically effective amount of at least one peptide with an amino acid sequence according to Formula II [AC-D-Nal(2).sup.1, D-Phe(4-Cl).sup.2, D-Pal(3).sup.3, D-Cit.sup.6, Nle.sup.7, Pro.sup.9, D-Ala.sup.10]-LHRH or a pharmaceutically acceptable salt thereof.

5. Method of claim 4, wherein said pharmaceutically effective amount of said at least one peptide is effective to protect T-lymphocytes infected with said virus.

6. The method of claim 4, wherein said pharmaceutically effective amount of said at least one peptide is effective to combat said virus by inhibiting proliferation of said virus.

7. A method of combating a virus that causes a disease selected from the group consisting of AIDS and ARC by administering a pharmaceutically effective amount of at least one peptide with an amino acid sequence according to Formula III [AC-D-Nal(2).sup.1, D-Phe(4-Cl).sup.2, D-Pal(3).sup.3, D-Cit.sup.6, Nva.sup.7, Pro.sup.9, D-Ala.sup.10]-LHRH or a pharmaceutically acceptable salt thereof.

8. The method of claim 7, wherein said pharmaceutically effective amount of said at least one peptide is effective to protect T-lymphocytes infected with said virus.

9. The method of claim 7, wherein said pharmaceutically effective amount of said at least one peptide is effective to combat said virus by inhibiting proliferation of said virus.

10. A method of combating a virus that causes a disease selected from the group consisting of AIDS and ARC by administering a pharmaceutically

effective amount of at least one peptide with an amino acid sequence according to Formula IV [AC-D-Nal(2).sup.1, D-Phe(4-Cl).sup.2, D-Trp.sup.3, D-Cit.sup.6, Pro.sup.9, D-Ala.sup.10]-LHRH or a pharmaceutically acceptable salt thereof.

11. The method of claim 10, wherein said pharmaceutically effective amount of said at least one peptide is effective to protect T-lymphocytes infected with said virus.

12. The method of claim 10, wherein said pharmaceutically effective amount of said at least one peptide is effective to combat said virus by inhibiting proliferation of said virus.

13. A method of combating a virus that causes a disease selected from the group consisting of AIDS and ARC by administering a pharmaceutically effective amount of at least one peptide with an amino acid sequence according to Formula V [AC-D-Nal(2).sup.1, D-Phe(4-Cl).sup.2, D-Pal(3).sup.3, D-Cit.sup.6, Pro.sup.9, D-Ala.sup.10]-LHRH or a pharmaceutically acceptable salt thereof.

14. The method of claim 13, wherein said pharmaceutically effective amount of said at least one peptide is effective to protect T-lymphocytes infected with said virus.

15. The method of claim 14, wherein said pharmaceutically effective amount of said at least one peptide is effective to combat said virus by inhibiting proliferation of said virus.

16. A method of combating a virus that causes a disease selected from the group consisting of AIDS and ARC by administering a pharmaceutically effective amount of at least one peptide with an amino acid sequence according to Formula VI [Ac-D-Nal(2).sup.1, D-Phe(4-Cl).sup.2, D-Pal(3).sup.3, D-Hci.sup.6, Pro.sup.9, D-Ala.sup.10]-LHRH or a pharmaceutically acceptable salt thereof.

17. The method of claim 16, wherein said pharmaceutically effective amount of said at least one peptide is effective to protect T-lymphocytes infected with said virus.

18. The method of claim 16, wherein said pharmaceutically effective amount of said at least one peptide is effective to combat said virus by inhibiting proliferation of said virus.

19. A method of combating a virus that causes a disease selected from the group consisting of AIDS and ARC by administering a pharmaceutically effective amount of at least one peptide with an amino acid sequence according to Formula VII [Ac-D-Nal(2).sup.1, D-Phe(4-Cl).sup.2, D-Pal(3).sup.3, D-Cit.sup.8, t-Leu.sup.7, Pro.sup.9, D-Ala.sup.10]-LHRH or a pharmaceutically acceptable salt thereof.

20. The method of claim 19, wherein said pharmaceutically effective amount of said at least one peptide is effective to protect T-lymphocytes infected with said virus.

21. The method of claim 19, wherein said pharmaceutically effective amount of said at least one peptide is effective to combat said virus by inhibiting proliferation of said virus.

22. A method of combating a virus that causes a disease selected from the group consisting of AIDS and ARC by administering a pharmaceutically effective amount of at least one peptide with an amino acid sequence according to Formula VII [Ac-D-Nal(2).sup.1, D-Phe(4-Cl).sup.2,

D-Pal(3).sup.3, D-Cit.sup.6, Ala.sup.9, D-Ala.sup.10]-LHRH or a pharmaceutically acceptable salt thereof.

23. The method of claim 22, wherein said pharmaceutically effective amount of said at least one peptide is effective to protect T-lymphocytes infected with said virus.

24. The method of claim 22, wherein said pharmaceutically effective amount of said at least one peptide is effective to combat said virus by inhibiting proliferation of said virus.

L13 ANSWER 10 OF 10 USPATFULL
CLM What is claimed is:

1. In an aerosol compressed gas package for administering a biologically active substance, comprising an aerosol container a propellant in said container and a biologically active substance dispersed in said propellant; the improvement in which said propellant also contains a member of the group consisting of polyoxyethylene-25glyceryl trioleate, polyoxyethylene-30-glyceryl monooleate and polyoxyethylene-20-glyceryl monooleate as suspension stabilizer and/or valve lubricant.

2. An aerosol compressed gas package as set forth in claim 1 in which the suspension stabilizer is polyoxyethylene-25-glyceryl trioleate.

3. An aerosol compressed gas package as set forth in any one of claim 1 in which the proportion of said suspension stabilizer relative to the total weight of the contents of said container is between 0.01 and 5 weight %.

4. An aerosol compressed gas package as set forth in claim 3 in which the proportion of said suspension stabilizer relative to the total weight of the contents of said container is between 0.2 and 2.5 weight %.

5. An aerosol compressed gas package as set forth in claim 3 in which the proportion of said suspension stabilizer relative to the total weight of the contents of said container is between 0.75 and 1.5 weight %.

6. An aerosol compressed gas packages according any one of claim 1 in which the propellant is at least one member of the group consisting of TG 227 and TG 134a.

```
=> s cetrorelix or lhrh antagonist or gnrh antagonist
L14       4916 CETRORELIX OR LHRH ANTAGONIST OR GNRH ANTAGONIST

=> s l14 and (prepar? or making or process?)
   6 FILES SEARCHED...
L15        875 L14 AND (PREPAR? OR MAKING OR PROCESS?)

=> s l15 and steril?
L16        160 L15 AND STERIL?

=> dup rem l16
PROCESSING COMPLETED FOR L16
L17         158 DUP REM L16 (2 DUPLICATES REMOVED)

=> s l17 and cetrorelix
L18         36 L17 AND CETRORELIX
```

=> d bib ab 1-36

L18 ANSWER 1 OF 36 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 2001132165 EMBASE
TI Gonadotropin-releasing hormone analogs stimulate and testosterone inhibits the recovery of spermatogenesis in irradiated rats.
AU Shetty G.; Wilson G.; Huhtaniemi I.; Shuttlesworth G.A.; Reissmann T.; Meistrich M.L.
CS G. Shetty, Dept. of Exp. Radiation Oncology, University of Texas, M. D. Anderson Cancer Center, Houston, TX 77030, United States. gshetty@audumla.mdacc.tmc.edu
SO Endocrinology, (2000) 141/5 (1735-1745).
Refs: 33
ISSN: 0013-7227 CODEN: ENDOAO
CY United States
DT Journal; Article
FS 003 Endocrinology
037 Drug Literature Index
LA English
SL English
AB We investigated the effects of GnRH analogs, different doses of testosterone (T), an androgen receptor antagonist (flutamide), and combinations of these on the recovery of spermatogenesis after irradiation. Treatment with a GnRH agonist (Lupron) for 10 weeks after irradiation reduced the intratesticular T concentration (ITT) to 4% of that in irradiated rats and serum FSH to undetectable levels without altering serum LH levels. Injection of a **GnRH antagonist** (**Cetrorelix**) at 3 weeks after irradiation suppressed LH, FSH, and ITT to <7%, 32%, and 10%, respectively, of levels in irradiated-only rats within 2 weeks; suppression was maintained for approximately 3 to 4 weeks. The percentage of tubules with differentiated germ cells (repopulation index, RI) was <0.6% at weeks 10 to 20 after irradiation. Spermatogenic recovery was induced by both the GnRH agonist (RI = 58% at week 10; 91% at week 20) and antagonist (RI = 70% at week 13). There was a dose-dependent suppression of testicular germ cell repopulation when T was combined with GnRH analogs. The ability of T to abolish the spermatogenic stimulatory effect of the **GnRH antagonist** was evident by the similar RI obtained for irradiated rats given antagonist + T or T alone. This suppression of GnRH-induced recovery of spermatogenesis by T could be reversed by flutamide. The RI best correlated with the degree of ITT suppression. In ITT-suppressed rats, the RI also showed an inverse correlation with serum T levels. Thus, T and/or its androgenic metabolites either directly or indirectly inhibit spermatogenic recovery after irradiation through an androgen receptor-mediated **process**. In addition, there was a close negative correlation between RI and FSH levels, and hence, a spermatogenic inhibitory role for FSH in the irradiated rats cannot be ruled out.

L18 ANSWER 2 OF 36 WPIDS (C) 2002 THOMSON DERWENT
AN 2002-351844 [38] WPIDS
DNC C2002-099958
TI Sustained release composition to treat central nervous system disorders comprises a water insoluble complex of a peptide and ligands, and a carrier macromolecule.
DC B04
IN GEFTER, M L
PA (PRAE-N) PRAECIS PHARM INC
CYC 96
PI WO 2002022154 A2 20020321 (200238)* EN 35p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO
RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW

ADT WO 2002022154 A2 WO 2001-US28691 20010913

PRAI US 2000-232188P 20000913

AB WO 200222154 A UPAB: 20020618

NOVELTY - A sustained release composition (I) comprises a water insoluble complex (WIC) of a peptide (II) and ligands (III) which are linked.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a composition comprising a water insoluble complex (WIC) of a peptide (II), ligands (III), each being negatively or positively charged, and an ionic carrier macromolecule (IV) linked to (III) having a charge opposite to the charge of (III);

(2) a composition comprising WIC of a peptide (II), ligands (III), each being positively charged, and carboxymethylcellulose;

(3) a composition comprising WIC of a charged active drug, and an ionic (IV) having a charge opposite to the charge of the drug; and

(4) **preparation** of the compositions.

ACTIVITY - Nootropic; Neuroprotective; Antiparkinsonian; Anticonvulsant; Hypotensive; Antidepressant; Tranquilizer; Antimigraine; Anorectic; Antiarteriosclerotic; Antiangial; Cytostatic; Antidiabetic; Antithyroid; Antiulcer; Antiinflammatory; Anti-HIV; Immunosuppressive; Nephrotropic.

MECHANISM OF ACTION - None given in the source material.

USE - The sustained delivery of peptides are used to treat central nervous system disorders, e.g. Alzheimer's disease, Parkinson's disease, multiple sclerosis, epilepsy, autonomic function disorders, e.g. hypertension, neuropsychiatric disorders, e.g. depression, anxiety, learning or memory disorders, e.g. amnesia, attention deficit disorder, migraine and obesity, cardiovascular disorders, e.g. arteriosclerosis, angina, cancer, diabetes mellitus, thyroid disorders, reproductive disorders, inflammatory or immune system disorders, e.g. ulcerative colitis, Crohn's disease, HIV, autoimmune disorders, gastrointestinal disorders and digestive disorders, e.g. peptic ulcers, metabolic disorders, and renal disorders, e.g. glumerulonephritis.

ADVANTAGE - The association of the peptide and ligands in a tight, stable complex allows for loading of high concentrations of peptide into the composition. The compositions also provide delivery of a peptide for prolonged periods of time, e.g. 1 month.

Dwg.0/2

L18 ANSWER 3 OF 36 WPIDS (C) 2002 THOMSON DERWENT

AN 2002-188161 [24] WPIDS

DNC C2002-058004

TI Water-in-oil microemulsion for parenteral administration of biologically active hydrophilic compounds to suppress production of e.g. testosterone, provides sustained release of the active compounds.

DC A96 B04 B07

IN AUTUORI, F; BIANCHINI, C; BOTTONI, G; LEONI, F; MASCAGNI, P; MONZANI, W; PICCOLO, O

PA (ITAF) ITALFARMACO SPA

CYC 96

PI WO 2001089479 A2 20011129 (200224)* EN 24p

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001081786 A 20011203 (200225)

ADT WO 2001089479 A2 WO 2001-EP5949 20010523; AU 2001081786 A AU 2001-81786 20010523
FDT AU 2001081786 A Based on WO 200189479
PRAI IT 2000-MI1173 20000526
AB WO 200189479 A UPAB: 20020416
NOVELTY - A stable, biologically compatible, well-tolerated water-in-oil microemulsion provides the sustained release of contained biologically active compounds.
USE - For the parenteral administration of biologically active hydrophilic compounds to suppress production of, e.g. testosterone or growth hormone (claimed).
ADVANTAGE - After administration to experiment animals, the inventive microemulsion induces no persistent ulcerations, and any swelling at the injection site is reversible. It is easy to **prepare** and free from remarkable systemic or topical side effects, and can be **sterilized.**
Dwg.0/2

L18 ANSWER 4 OF 36 WPIDS (C) 2002 THOMSON DERWENT
AN 2002-075276 [10] WPIDS
DNC C2002-022462
TI Stable solution/dispersion for parenteral administration of peptides subject to aggregation, for treating hormone-dependent diseases, contains specific salt of peptide and corresponding acid.
DC A96 B04
IN BAUER, H; DAMM, M; SARLIKIOTIS, W
PA (ZENT-N) ZENTARIS AG; (ASTA) ASTA MEDICA AG; (BAUE-I) BAUER H; (DAMM-I) DAMM M; (SARL-I) SARLIKIOTIS W
CYC 57
PI WO 2001087265 A2 20011122 (200210)* DE 16p
RW: AT BE CH CY DE DK EA ES FI FR GB GR IE IT LU MC NL PT SE TR
W: AU BG BR BY CA CN CO CZ EE GE HR HU ID IL IN IS JP KG KR KZ LT LV MK MX NO NZ PL RO RU SG SI SK TR UA UZ YU ZA
CA 2348167 A1 20011118 (200210) EN
DE 10024451 A1 20011129 (200210)
AU 2001074041 A 20011126 (200222)
US 2002039996 A1 20020404 (200227)
ADT WO 2001087265 A2 WO 2001-EP5555 20010516; CA 2348167 A1 CA 2001-2348167 20010518; DE 10024451 A1 DE 2000-10024451 20000518; AU 2001074041 A AU 2001-74041 20010516; US 2002039996 A1 US 2001-861009 20010518
FDT AU 2001074041 A Based on WO 200187265
PRAI DE 2000-10024451 20000518
AB WO 200187265 A UPAB: 20020213
NOVELTY - Pharmaceutical dosage form (A) for the parenteral administration of peptides (I), present in dissolved or dispersed from and tending to aggregate, contains:
(a) (I) in the form of its acetate, gluconate, glucuronate, lactate, citrate, ascorbate, benzoate or phosphate salt;
(b) a free acid corresponding to one of the above salts and optionally
(c) acids, surfactants, polymers, lipids or sugars.
DETAILED DESCRIPTION - Pharmaceutical dosage form (A) for the parenteral administration of peptides (I), present in dissolved or dispersed from and tending to aggregate, contains:
(a) (I) in the form of its acetate, gluconate, glucuronate, lactate, citrate, ascorbate, benzoate or phosphate salt;
(b) a free acid corresponding to one of the above salts and optionally
(c) further additives selected from acids, surfactants, polymers, lipids or sugars.
INDEPENDENT CLAIMS are included for the **preparation** of (A).
ACTIVITY - Cytostatic; Gynecological; Antifertility; Antinfertility.

MECHANISM OF ACTION - Luteinizing hormone releasing hormone (**LHRH**) **antagonist.**

USE - Used for the treatment of sexual hormone-dependent, benign or malignant diseases, especially benign prostate hyperplasia, prostate carcinoma, precocious puberty, hirsutism, endometrial hyperplasia or associated symptoms, premenstrual syndrome, uterine myomatosis, breast cancer, tubal obstruction, ovarian cancer or uterine carcinoma, or in contraception or in vitro fertilization.

ADVANTAGE - (A) Are stable injectable **preparations** for rapid or retarded release of (I), which have acceptable bioavailability and are readily **prepared, sterile**-filtered and stored. Problems of insufficient release rate or bioavailability due to aggregation of (I) are eliminated.

Dwg.0/0

L18 ANSWER 5 OF 36 WPIDS (C) 2002 THOMSON DERWENT
AN 2000-565259 [52] WPIDS
DNC C2000-168330
TI Pharmaceutical composition for sustained delivery of an active peptidic compound, such as a luteinising hormone-releasing hormone antagonist comprises a water-insoluble salt.
DC A96 B04 B07
IN BAUER, H; DAMM, M; DEGER, W; SARLIKIOTIS, W; DANN, M
PA (ASTA) ASTA MEDICA AG; (ZENT-N) ZENTARIS AG
CYC 56
PI WO 2000047234 A1 20000817 (200052)* EN 23p
RW: AT BE CH CY DE DK EA ES FI FR GB GR IE IT LU MC NL PT SE
W: AU BG BR BY CA CN CZ EE GE HR HU ID IL IN IS JP KG KR KZ LT LV MK MX NO NZ PL RO RU SG SI SK TR UA UZ YU ZA
AU 2000027997 A 20000829 (200062)
EP 1150717 A1 20011107 (200168) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
NO 2001003851 A 20010928 (200170)
BR 2000008786 A 20011106 (200175)
CZ 2001002841 A3 20020313 (200223)
ZA 2001006467 A 20020227 (200223) 38p
SK 2001001131 A3 20020404 (200232)
ADT WO 2000047234 A1 WO 2000-EP697 20000129; AU 2000027997 A AU 2000-27997 20000129; EP 1150717 A1 EP 2000-906245 20000129, WO 2000-EP697 20000129; NO 2001003851 A WO 2000-EP697 20000129, NO 2001-3851 20010807; BR 2000008786 A BR 2000-8786 20000129, WO 2000-EP697 20000129; CZ 2001002841 A3 WO 2000-EP697 20000129, CZ 2001-2841 20000129; ZA 2001006467 A ZA 2001-6467 20010807; SK 2001001131 A3 WO 2000-EP697 20000129, SK 2001-1131 20000129
FDT AU 2000027997 A Based on WO 200047234; EP 1150717 A1 Based on WO 200047234; BR 2000008786 A Based on WO 200047234; CZ 2001002841 A3 Based on WO 200047234; SK 2001001131 A3 Based on WO 200047234
PRAI US 1999-119076P 19990208
AB WO 200047234 A UPAB: 20001018

NOVELTY - A pharmaceutical composition (I) comprising a water-insoluble salt of a pharmaceutically active ionic peptidic compound (PC) and a counterionic carrier macromolecule (CM), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a pharmaceutical composition (II) comprising a water-insoluble salt consisting essentially of a pharmaceutically active PC and a CM; and

(2) **preparing** a pharmaceutical formulation comprising a PC and a CM comprises:

(i) forming the free ions of both compounds by removing the counter ions;

(ii) combining the ionic PC and the ionic CM under conditions such

that a water-insoluble salt of the PC and the CM forms; and

(iii) **preparing** a pharmaceutical formulation comprising the water insoluble salt.

ACTIVITY - None given.

MECHANISM OF ACTION - None given.

USE - (I) is used for sustained delivery of an active PC, such as a luteinising hormone-releasing hormone (**LHRH**) **antagonist** that is **cetrorelix**, teverelix, abarelix, ganirelix RS-26306, azaline B, antide ORF-23541, A-75998, detirelix RS-68439, ramorelix HOE-2013, or Nal-Glu ORF-21234.

ADVANTAGE - (I) can permit continuous delivery of an active PC to a subject for prolonged periods of time, e.g. one month. The association of the PC with the CM is a tight stable complex which allows loading of high concentrations of the PC into the formulation.

Dwg.0/2

L18 ANSWER 6 OF 36 WPIDS (C) 2002 THOMSON DERWENT
AN 1999-579322 [49] WPIDS
CR 1998-193308 [17]
DNC C1999-168473
TI **Preparation** of pharmaceutical implants containing active biopeptides or analogs in a lactic acid/ glycolic acid copolymer carrier - uses aqueous slurry to wet the active component prior to blending with copolymer.
DC A23 A96 B04 B07 D22
IN DEGHENGHI, R
PA (DEGH-I) DEGHENGHI R
CYC 1
PI US 5945128 A 19990831 (199949)* 7p
ADT US 5945128 A Provisional US 1996-25449 19960904, US 1997-897942 19970721
PRAI US 1996-25449 19960904; US 1997-897942 19970721
AB US 5945128 A UPAB: 19991124

NOVELTY - A **process** for incorporating an active biopeptide or analog into a long term release pharmaceutical implant having a lactic acid/ glycolic acid copolymer carrier using an aqueous slurry of active component is new

DETAILED DESCRIPTION - A **process** for **making** pharmaceutical implants capable of delivering a bioactive peptide or peptide analogue over 1-12 months comprises:

(1) grinding a lactic acid/ glycolic acid copolymer, where the lactic acid : glycolic acid ratio is 0-5:1, to a particle size of 50-150 micro m;

(2) wetting the **sterilized** copolymer with a **sterile** aqueous slurry of the active component:

(3) blending the copolymer and the slurry to a homogenous mixture containing 10-50 % active component;

(4) drying the mixture under reduced pressure at less than 25 deg. C;

(5) extruding the dried mixture at 70-110 deg. C; and

(6) cutting the extrusion into cylindrical implant rods that are 1-2 mm in diameter and 10-25 mm long.

USE - Used in the manufacture of pharmaceutical implants especially for the prolonged administration of drugs such as antagonists or agonists of Leuteinizing Hormone Releasing Hormone (LHRH), Gonadotrophin Releasing Hormone (GnRH), growth hormone releasing hormone, growth hormone releasing polypeptide, angiotensin, bombesin, bradykinin, cholecystokinin, enkephalin, neurokinin, tachykinin or Substance P; inhibitors of renin, proteases, metalloproteases, enkephalinase and atrial or brain natriuretic factor degrading enzyme. The method is also suitable for the manufacture of implants containing leuprolide, goserelin, triptorelin, buserelin, avorelin, deslorelin, histrelin, **cetrorelix**, teverelix, ramorelix, antide, nictide, azeline B, azeline C and ganirelix.

ADVANTAGE - The formulations are not contaminated with organic solvents such as chloroform and methylene chloride and the use of water

helps to achieve a uniform distribution of the drug. The powdery mixture is wettable to aid the manufacturing **process** and allows **sterilization** of the active ingredient prior to mixture with the polymer.
Dwg.0/3

L18 ANSWER 7 OF 36 WPIDS (C) 2002 THOMSON DERWENT
AN 1994-265229 [33] WPIDS
DNC C1994-121294
TI Freeze-dried peptide compsns. - prepd. by freeze drying soln. of peptide in aq. acetic acid.
DC B04
IN ENGEL, J; REISSMANN, T; SAUERBIER, D; WICHERT, B; BURKHARD, W; JUERGEN, E
PA (ASTA) ASTA MEDICA AG
CYC 32
PI EP 611572 A2 19940824 (199433)* DE 5p
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
DE 4305225 A1 19940825 (199433) 5p
AU 9455235 A 19940825 (199436)
NO 9400564 A 19940822 (199436)
CA 2115943 A 19940820 (199439)
CZ 9400312 A3 19940914 (199439)
BR 9400617 A 19940927 (199440)
SK 9400195 A3 19940907 (199440)
FI 9400779 A 19940820 (199441)
JP 06271476 A 19940927 (199443) 5p
ZA 9401136 A 19941026 (199444) 12p
HU 67117 T 19950228 (199514)
EP 611572 A3 19950111 (199538)
AU 671881 B 19960912 (199644)
CN 1112019 A 19951122 (199737)
SG 46632 A1 19980220 (199822)
BR 1101004 A3 19980512 (199828)
CZ 284314 B6 19981014 (199847)
NZ 314707 A 19990225 (199914)
CZ 285768 B6 19991117 (200002)
EP 611572 B1 20000607 (200032) DE
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
DE 59409389 G 20000713 (200037)
HU 218281 B 20000728 (200045)
RU 2145234 C1 20000210 (200048)
ES 2148247 T3 20001016 (200058)
TW 387812 A 20000421 (200061)
ADT EP 611572 A2 EP 1994-101672 19940204; DE 4305225 A1 DE 1993-4305225 19930219; AU 9455235 A AU 1994-55235 19940217; NO 9400564 A NO 1994-564 19940218; CA 2115943 A CA 1994-2115943 19940218; CZ 9400312 A3 CZ 1994-312 19940214; BR 9400617 A BR 1994-617 19940218; SK 9400195 A3 SK 1994-195 19940218; FI 9400779 A FI 1994-779 19940218; JP 06271476 A JP 1994-20532 19940217; ZA 9401136 A ZA 1994-1136 19940218; HU 67117 T HU 1994-481 19940218; EP 611572 A3 EP 1994-101672 19940204; AU 671881 B AU 1994-55235 19940217; CN 1112019 A CN 1994-101378 19940218; SG 46632 A1 SG 1996-6874 19940204; BR 1101004 A3 BR 1997-1101004 19970514; CZ 284314 B6 CZ 1994-312 19940214; NZ 314707 A Div ex NZ 1994-250906 19940217, NZ 1994-314707 19940217; CZ 285768 B6 CZ 1998-974 19940214; EP 611572 B1 EP 1994-101672 19940204, Related to EP 1999-102340 19940204; DE 59409389 G DE 1994-509389 19940204, EP 1994-101672 19940204; HU 218281 B HU 1994-481 19940218; RU 2145234 C1 RU 1994-5001 19940218; ES 2148247 T3 EP 1994-101672 19940204; TW 387812 A TW 1994-100769 19940131
FDT AU 671881 B Previous Publ. AU 9455235; CZ 284314 B6 Previous Publ. CZ 9400312; NZ 314707 A Div ex NZ 250906; CZ 285768 B6 Previous Publ. CZ 9800974; EP 611572 B1 Related to EP 947200; DE 59409389 G Based on EP 611572; HU 218281 B Previous Publ. HU 67117; ES 2148247 T3 Based on EP

611572
PRAI DE 1993-4305225 19930219
AB EP 611572 A UPAB: 19991110
Freeze-dried compsns. comprising a peptide of 3-15 amino acid units and opt. one or more matrix materials are characterised in that 1 pt. wt. of the peptide is dissolved in 100-10,000 pts. wt. of acetic acid and then transferred to water and the resulting soln. is freeze dried.
USE/ADVANTAGE - The compsns. esp. contain **cetrorelix** (EP 299402), which is used in the treatment of female infertility (for controlling ovulation prior to isolating egg cells for in-vitro fertilisation) and for gonad protection in male patients (e.g. undergoing ratio- or chemotherapy). The aq. acetic acid soln. can be **sterilised** by filtration without gelation or hydrolysis of the peptide.
Dwg.0/0

L18 ANSWER 8 OF 36 CAPLUS COPYRIGHT 2002 ACS
AN 2002:142735 CAPLUS
DN 136:189380
TI Method for producing peptide salts, their use, and pharmaceutical **preparations** containing these peptide salts in relation to **cetrorelix** embonate
IN Damm, Michael; Salonek, Waldemar; Engel, Juergen; Bauer, Horst; Stach, Gabriele
PA Zentaris A.-G., Germany
SO PCT Int. Appl., 10 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002014347	A2	20020221	WO 2001-EP9219	20010809
W: AU, BG, BR, BY, CA, CN, CO, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, UZ, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
DE 10040700	A1	20020228	DE 2000-10040700	20000817

PRAI DE 2000-10040700 A 20000817
AB The invention relates to pharmaceutical prepns. contg. peptide salt, to their prodn., and to the use as injections. The invention particularly relates to pharmaceutical prepns. contg. a slightly sol. salt of LHRH agonists or antagonists such as **cetrorelix** embonate for the parenteral administration in mammals with a long-sustained action. Thus 46.47 g D 20761 (**Cetrorelix** acetate) was dissolved in 1193 water; 3261 g 96% ethanol was added, filtered and mixed with 390 g Amberlite MB3 (mixed-bed cation-anion-exchanger). After treatment the resin was filtered; to 4162 g of the supernatant 5.34 g embonic acid were added. 3333 G of the **Cetrorelix** embonate soln. was **sterile** filtrated and mixed with 528 g mannitol soln. (316.8 g mannite was dissolved previously in 1267 g water), **sterilized** and filled in ampules and lyophilized.

L18 ANSWER 9 OF 36 CAPLUS COPYRIGHT 2002 ACS
AN 1998:169441 CAPLUS
DN 128:235145
TI Pharmaceutical implants containing bioactive peptides
IN Deghenghi, Romano
PA Deghenghi, Romano, Switz.
SO PCT Int. Appl., 18 pp.
CODEN: PIXXD2

DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9809613	A1	19980312	WO 1997-EP4095	19970728
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 5945128	A	19990831	US 1997-897942	19970721
	CA 2236595	AA	19980312	CA 1997-2236595	19970728
	AU 9740121	A1	19980326	AU 1997-40121	19970728
	AU 713123	B2	19991125		
	EP 858323	A1	19980819	EP 1997-937521	19970728
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	CN 1200032	A	19981125	CN 1997-191184	19970728
	BR 9706741	A	19990720	BR 1997-6741	19970728
	JP 11514678	T2	19991214	JP 1998-512154	19970728
	US 6077523	A	20000620	US 1999-311744	19990514
	US 6159490	A	20001212	US 2000-543707	20000405
PRAI	US 1996-25444P	P	19960904		
	US 1997-897942	A	19970721		
	WO 1997-EP4095	W	19970728		
	US 1999-311744	A1	19990514		

AB A **process** for manufg. a pharmaceutical compn. for the delivery of an effective amt. of a bioactive peptide or peptide analog over a period of 1 to 12 mo is disclosed. This **process** includes the steps of grinding a copolymer of lactic acid and glycolic acid having a ratio of glycolide to lactide units of from about 0 to 5:1 to a particle size of between about 50 and 150 .mu.m; **sterilizing** the ground copolymer with a dose of between about 1 and 2.5 Mrads of ionizing .gamma.-radiation; wetting the ground and **sterilized** copolymer with a **sterile** aq. slurry of a bioactive peptide or peptide analog; aseptically blending the copolymer and the slurry to obtain a homogeneous mixt. of the copolymer and between about 10 and 50 % of the bioactive peptide or peptide analog; drying the mixt. at reduced pressure and at temp. not exceeding 25.degree.C; aseptically extruding the dried mixt. at a temp. between about 70 and 110.degree.C; and aseptically cutting cylindrical rods of about 1 to 2 mm diam. and between about 10 and 25 mm in length from the extruded mixt. to form the pharmaceutical implants. Pharmaceutical rods for s.c. implant, 1.5 mm diam. and 15 mm long, contg. 10 mg avorelin were prepd. according to above method and were implanted in dogs. After the initial stimulation of LH and testosterone, castration levels of testosterone were maintained for 6 mo. The plasma levels of avorelin, after a short-lived burst, fell to a nadir at 40 day days and rose again at 120 days before becoming undetectable at day 160.

L18 ANSWER 10 OF 36 USPATFULL
AN 2002:112303 USPATFULL
TI Methods for treating FSH related conditions with GnRH antagonists
IN Garnick, Marc B., Brookline, MA, UNITED STATES
Martha, Paul M., JR., Topsfield, MA, UNITED STATES
Molineaux, Christopher J., San Mateo, CA, UNITED STATES
DePaoli, Alex, Santa Barbara, CA, UNITED STATES
PI US 2002058035 A1 20020516
AI US 2001-793669 A1 20010227 (9)

PRAI US 2000-185573P 20000228 (60)
US 2000-185574P 20000228 (60)
US 2000-238337P 20001005 (60)
US 2000-238338P 20001005 (60)
DT Utility
FS APPLICATION
LREP LAHIVE & COCKFIELD, 28 STATE STREET, BOSTON, MA, 02109
CLMN Number of Claims: 59
ECL Exemplary Claim: 1
DRWN 5 Drawing Page(s)
LN.CNT 1529
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods for treating FSH related conditions, such as prostatic intraepithelial neoplasia, pedophilia, infertility, or vaginal bleeding, with GnRH antagonists are disclosed. The methods of the invention generally feature administering to a subject a **GnRH antagonist** suitable for in vivo administration and able to reduce both plasma FSH and LH levels in a subject, in an amount or in a formulation effective to reduce plasma FSH levels in the subject to a symptom alleviating level. In vitro fertilization and male contraceptive methods are also provided.

L18 ANSWER 11 OF 36 USPATFULL
AN 2002:72856 USPATFULL
TI Pharmaceutical administration form for peptides, **process** for its **preparation**, and use
IN Bauer, Horst, Hersbruck, GERMANY, FEDERAL REPUBLIC OF
Damm, Michael, Rodermark, GERMANY, FEDERAL REPUBLIC OF
Sarlikiotis, Werner, Peania, GREECE
PI US 2002039996 A1 20020404
AI US 2001-861009 A1 20010518 (9)
PRAI DE 2000-10024451 20000518
DT Utility
FS APPLICATION
LREP GABGRIEL P. KATONA L.L.P., 14th Floor, 708 Third Avenue, New York, NY, 10017
CLMN Number of Claims: 17
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 571
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to pharmaceutical administration forms suitable for parenteral administration, which contains [sic] peptides prone to aggregation in the form of their acetate, gluconate, glucuronate, lactate, citrate, ascorbate, benzoate or phosphate salts in dissolved or dispersed form and additionally comprises [sic] one of the acids mentioned as free acid.

L18 ANSWER 12 OF 36 USPATFULL
AN 2002:72457 USPATFULL
TI SOLID POROUS MATRICES AND METHODS OF **MAKING** AND USING THE SAME
IN UNGER, EVAN C., TUCSON, AZ, UNITED STATES
PI US 2002039594 A1 20020404
AI US 1998-75477 A1 19980511 (9)
PRAI US 1997-46379P 19970513 (60)
DT Utility
FS APPLICATION
LREP WOODCOCK WASHBURN KURTZ, MACKIEWICZ AND NORRIS, ONE LIBERTY PLACE 46TH FLOOR, PHILADELPHIA, PA, 19103
CLMN Number of Claims: 106
ECL Exemplary Claim: 1
DRWN 1 Drawing Page(s)

LN.CNT 5207
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention is directed to a solid porous matrix comprising a solvent and a surfactant in combination with a bioactive agent. The solvent and the surfactant may, if desired, form vesicles, an agglomeration of which comprises the matrix. The composition optionally comprises a gas or a gaseous precursor. The emulsion may be dried, and subsequently reconstituted in an aqueous or organic solution.

The present invention is also directed to a method of **preparing** a solid porous matrix comprising combining a solvent, a surfactant, and a therapeutic to form an emulsion; and **processing** the emulsion by controlled drying, or controlled agitation and controlled drying to form a solid porous matrix. The resulting solid porous matrix may also comprise a gas or gaseous precursor and be added to a resuspending medium.

A method for the controlled delivery of a targeted therapeutic to a region of a patient is another embodiment of the present invention. The method comprises administering to the patient a composition having a solid porous matrix comprising a solvent, a surfactant, a therapeutic, and a gas or gaseous precursor, monitoring the composition using energy to determine the presence of the composition in the region; and releasing the therapeutic from the composition in the region using energy.

L18 ANSWER 13 OF 36 USPATFULL
AN 2002:61254 USPATFULL
TI Compositions and methods for the treatment of cancer
IN Zeldis, Jerome B., Princeton, NJ, UNITED STATES
Zeitlin, Andrew L., Basking Ridge, NJ, UNITED STATES
Barer, Sol, Westfield, NJ, UNITED STATES
PI US 2002035090 A1 20020321
AI US 2001-853617 A1 20010514 (9)
PRAI US 2000-204143P 20000515 (60)
DT Utility
FS APPLICATION
LREP PENNIE & EDMONDS LLP, 1667 K STREET NW, SUITE 1000, WASHINGTON, DC, 20006
CLMN Number of Claims: 60
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1973
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention relates to compositions comprising thalidomide and another anti-cancer drug which can be used in the treatment or prevention of cancer. Preferred anti-cancer drugs are topoisomerase inhibitors. A particular composition comprises thalidomide, or a pharmaceutically acceptable salt, solvate, or clathrate thereof, and irinotecan. The invention also relates to methods of treating or preventing cancer which comprise the administration of a thalidomide and another anti-cancer drug to a patient in need of such treatment or prevention. The invention further relates to methods of reducing or avoiding adverse side effects associated with the administration of chemotherapy or radiation therapy which comprise the administration of thalidomide to a patient in need of such reduction or avoidance.

L18 ANSWER 14 OF 36 USPATFULL
AN 2002:54993 USPATFULL
TI Pharmaceutical combined **preparation** and its use in the treatment of gynaecological disorders
IN Stockemann, Klaus, Berlin, GERMANY, FEDERAL REPUBLIC OF

Muhn, Peter, Berlin, GERMANY, FEDERAL REPUBLIC OF
PI US 2002032156 A1 20020314
AI US 2001-925419 A1 20010810 (9)
RLI Continuation of Ser. No. US 2000-658113, filed on 8 Sep 2000, ABANDONED
Continuation of Ser. No. US 1998-117357, filed on 22 Sep 1998, PENDING
PRAI DE 1996-19604231 19960129
DT Utility
FS APPLICATION
LREP MILLEN, WHITE, ZELANO & BRANIGAN, P.C., 2200 CLARENDON BLVD., SUITE 1400, ARLINGTON, VA, 22201
CLMN Number of Claims: 15
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 343
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to a pharmaceutical combined **preparation** of LHRH analogues and anti-oestrogens having tissue-selective oestrogen activity and also to its use for the treatment of gynaecological disorders, especially for the treatment of endometrioses and myomas.

L18 ANSWER 15 OF 36 USPATFULL
AN 2002:27450 USPATFULL
TI Somatostatin antagonists and agonists that act at the sst subtype 2 receptor
IN Hay, Bruce A., East Lyme, CT, UNITED STATES
Ricketts, Anthony P., Stonington, CT, UNITED STATES
Cole, Bridget M., Stonington, CT, UNITED STATES
PI US 2002016298 A1 20020207
AI US 2000-747437 A1 20001221 (9)
RLI Continuation-in-part of Ser. No. US 2000-618029, filed on 17 Jul 2000, PENDING
PRAI US 1999-151830P 19990901 (60)
DT Utility
FS APPLICATION
LREP Paul H. Ginsburg, Pfizer Inc., 20th Floor, 235 East 42nd Street, New York, NY, 10017-5755
CLMN Number of Claims: 27
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1886
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds according to the formula: ##STR1##

and pharmaceutically acceptable salts, solvates or hydrates thereof; wherein group Ar is optionally substituted (C.sub.6-C.sub.10)aryl or (C.sub.1-C.sub.9)heteroaryl; X is a direct link, --CH.sub.2--, --SO.sub.2--, --CO--, --CHR.sup.1-- where R.sup.1 is(C.sub.1-C.sub.6) alkyl, or --CR.sup.1'R.sup.1"-- where both R.sup.1' and R.sup.1" are, independently, (C.sub.1-C.sub.6)alkyl; Y is N or CH; and Z and W are as herein defined, and pharmaceutical compositions thereof, and methods useful to facilitate secretion of growth hormone(GH) in mammals.

L18 ANSWER 16 OF 36 USPATFULL
AN 2002:17328 USPATFULL
TI Dha-pharmaceutical agent conjugates of taxanes
IN Shashoua, Victor, Brookline, MA, UNITED STATES
Swindell, Charles, Merion, PA, UNITED STATES
Webb, Nigel, Bryn Mawr, PA, UNITED STATES
Bradley, Matthews, Layton, PA, UNITED STATES
PI US 2002010208 A1 20020124
AI US 2001-846838 A1 20010501 (9)
RLI Continuation of Ser. No. US 1998-135291, filed on 17 Aug 1998, ABANDONED

Continuation of Ser. No. US 1996-651312, filed on 22 May 1996, GRANTED, Pat. No. US 5795909
DT Utility
FS APPLICATION
LREP Edward R. Gates, Esq., Wolf, Greenfield & Sacks, P.C., 600 Atlantic Avenue, Boston, MA, 02210
CLMN Number of Claims: 19
ECL Exemplary Claim: 1
DRWN 14 Drawing Page(s)
LN.CNT 2437
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides conjugates of cis-docosahexaenoic acid and pharmaceutical agents useful in treating noncentral nervous system conditions. Methods for selectively targeting pharmaceutical agents to desired tissues are provided.

L18 ANSWER 17 OF 36 USPATFULL
AN 2002:14003 USPATFULL
TI Thienopyrimidine compounds, their production and use
IN Furuya, Shuichi, Tsukuba, JAPAN
Suzuki, Nobuhiro, Tsukuba, JAPAN
Choh, Nobuo, Tsukuba, JAPAN
Nara, Yoshi, Suita, JAPAN
PA Takeda Chemical Industries, Ltd., Osaka, JAPAN (non-U.S. corporation)
PI US 6340686 B1 20020122
AI US 2000-571215 20000516 (9)
RLI Continuation of Ser. No. US 530495
PRAI JP 1999-79371 19990324
JP 2000-18019 20000125
DT Utility
FS GRANTED
EXNAM Primary Examiner: Ford, John M.
LREP Chao, Mark, Ramesh, Elaine M.
CLMN Number of Claims: 24
ECL Exemplary Claim: 1
DRWN 1 Drawing Figure(s); 1 Drawing Page(s)
LN.CNT 1944
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A compound of the formula: ##STR1##

wherein R.sup.1 and R.sup.2 each is hydrogen, hydroxy, C.sub.1-4 alkoxy, C.sub.1-4 alkoxy-carbonyl or C.sub.1-4 alkyl which may be substituted; R.sup.3 is hydrogen, halogen, hydroxy or C.sub.1-4 alkoxy which may be substituted; or adjacent two R.sup.3 may form C.sub.1-4 alkylenedioxy; R.sup.4 is hydrogen or C.sub.1-4 alkyl; R.sup.6 is C.sub.1-4 alkyl which may be substituted or a group of the formula: ##STR2##

wherein R.sup.5 is hydrogen or R.sup.4 and R.sup.5 may form heterocycle; and n is 0-5, or a salt thereof, has an excellent GnRH-antagonizing activity, and is useful for preventing or treating sex hormone-dependent diseases.

L18 ANSWER 18 OF 36 USPATFULL
AN 2001:218538 USPATFULL
TI Somatostatin antagonists and agonists that act at the SST subtype 2 receptor
IN Hay, Bruce A., East Lyme, CT, United States
Cole, Bridget M., Stonington, CT, United States
Ricketts, Anthony P., Stonington, CT, United States
PI US 2001047030 A1 20011129
AI US 2000-734789 A1 20001212 (9)
PRAI US 2000-200319P 20000428 (60)

DT Utility
FS APPLICATION
LREP Paul H. Ginsburg, Pfizer Inc, 20th Floor, 235 East 42nd Street, New York, NY, 10017-5755
CLMN Number of Claims: 38
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1872
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds according formula (I)

A--G--Z--W

and pharmaceutically acceptable salts, solvates or hydrates thereof; wherein,

A is (C.sub.6-C.sub.10)aryl, (C.sub.6-C.sub.10)aryl-SO.sub.2, (C.sub.6-C.sub.10)aryl-CH.sub.2--, (C.sub.6-C.sub.10)arylcarbonyl, (C.sub.1-C.sub.9)heteroaryl, (C.sub.1-C.sub.9)heteroaryl-SO.sub.2--, (C.sub.1-C.sub.9)heteroaryl-CH.sub.2--; or (C.sub.1-C.sub.9)heteroarylcarbonyl;

G is selected from the group consisting of: ##STR1##

where B is (C.sub.6-C.sub.10)aryl or (C.sub.1-C.sub.9)heteroaryl, and X is CH.sub.2, SO.sub.2, or carbonyl; ##STR2##

where X is CH.sub.2, SO.sub.2, or carbonyl; and R.sup.1 and R.sup.1' are each independently selected from H, CN, (C.sub.1-C.sub.8)alkyl-, and phenyl(CH.sub.2)--, wherein said alkyl and phenyl groups are optionally substituted; and ##STR3##

where Z and W are as defined in the present Specificiation; and pharmaceutical compositions and methods useful to increase secretion of growth hormone(GH) from the anterior pituitary of mammals, including on a sustained release basis.

L18 ANSWER 19 OF 36 USPATFULL
AN 2001:218530 USPATFULL
TI Treatment or prevention of prostate cancer with a COX-2 selective inhibiting drug
IN Waldstreicher, Joanne, Scotch Plains, NJ, United States
Morrison, Briggs W., Watchung, NJ, United States
PI US 2001047022 A1 20011129
AI US 2001-771315 A1 20010126 (9)
PRAI US 2000-178722P 20000128 (60)
DT Utility
FS APPLICATION
LREP MERCK AND CO INC, P O BOX 2000, RAHWAY, NJ, 070650907
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 295
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A COX-2 selective inhibiting drug is disclosed as useful in treating or preventing prostate cancer. The compound is used alone or in combination with other drugs.

L18 ANSWER 20 OF 36 USPATFULL
AN 2001:205920 USPATFULL
TI Treatment or prevention of prostate cancer with a COX-2 selective inhibiting drug

IN Waldstreicher, Joanne, Scotch Plains, NJ, United States
Morrison, Briggs W., Watchung, NJ, United States
PI US 2001041713 A1 20011115
AI US 2001-784878 A1 20010216 (9)
PRAI US 2000-183204P 20000217 (60)
DT Utility
FS APPLICATION
LREP MERCK AND CO INC, P O BOX 2000, RAHWAY, NJ, 070650907
CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 295
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A COX-2 selective inhibiting drug is disclosed as useful in treating or preventing prostate cancer. The compound is used alone or in combination with other drugs.

L18 ANSWER 21 OF 36 USPATFULL
AN 2001:205879 USPATFULL
TI COMBINED PHARMACEUTICAL **PREPARATION** CONTAINING LHRH-ANALOGOUS SUBSTANCES AND ANTI ESTROGENS FOR TREATING GYNAECOLOGICAL DISORDERS
IN STOCKEMANN, KLAUS, BERLIN, Germany, Federal Republic of
MUHN, PETER, BERLIN, Germany, Federal Republic of
PI US 2001041672 A1 20011115
AI US 1998-117357 A1 19980922 (9)
WO 1997-EP395 19970129
None PCT 102(e) date
PRAI DE 1996-19604231 19960129
DT Utility
FS APPLICATION
LREP MILLEN WHITE ZELANO & BRANIGAN, ARLINGTON COURTHOUSE PLAZA I, 2200 CLARENDON BOULEVARD, SUITE 1400, ARLINGTON, VA, 22201
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 310
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to a pharmaceutical combined **preparation** of LHRH analogues and anti-oestrogens having tissue-selective oestrogen activity and also to its use for the treatment of gynaecological disorders, especially for the treatment of endometrioses and myomas.

L18 ANSWER 22 OF 36 USPATFULL
AN 2001:168259 USPATFULL
TI Thienopyrimidine compounds, their production and use
IN Furuya, Shuichi, Ibaraki, Japan
Suzuki, Nobuhiro, Ibaraki, Japan
Choh, Nobuo, Ibaraki, Japan
Nara, Yoshi, Osaka, Japan
PA Takeda Chemical Industries, Ltd., Osaka, Japan (non-U.S. corporation)
PI US 6297379 B1 20011002
WO 2000056739 20000928
AI US 2000-530495 20000426 (9)
WO 2000-JP1777 20000323
20000426 PCT 371 date
20000426 PCT 102(e) date
PRAI JP 1999-79371 19990324
DT Utility
FS GRANTED
EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: Rao, Deepak R.
LREP Riesen, Philippe Y., Chao, Mark
CLMN Number of Claims: 1

ECL Exemplary Claim: 1
DRWN 1 Drawing Figure(s); 1 Drawing Page(s)
LN.CNT 1679
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB ##STR1##

A compound of formula (I) wherein R.sup.1 and R.sup.2 each is hydrogen, hydroxy, C.sub.1-4 alkoxy, C.sub.1-4 alkoxy-carbonyl or C.sub.1-4 alkyl which may be substituted; R.sup.3 is hydrogen, halogen, hydroxy or C.sub.1-4 alkoxy which may be substituted; or adjacent two R.sup.3 may form C.sub.1-4 alkylenedioxy; R.sup.4 is hydrogen or C.sub.1-4 alkyl; R.sup.6 is C.sub.1-4 alkyl which may be substituted or a group of the formula (A) wherein R.sup.5 is hydrogen of R.sup.4 and R.sup.5 may form heterocycle; and n is 0-5, or a salt thereof, has an excellent GnRH-antagonizing activity, and is useful for preventing or treating sex hormone-dependent diseases.

L18 ANSWER 23 OF 36 USPATFULL
AN 2001:144937 USPATFULL
TI Solid matrix therapeutic compositions
IN Unger, Evan C., Tucson, AZ, United States
PA ImaRx Therapeutics, Inc. (U.S. corporation)
PI US 2001018072 A1 20010830
AI US 2001-828762 A1 20010409 (9)
RLI Division of Ser. No. US 1998-75477, filed on 11 May 1998, PENDING
PRAI US 1997-46379P 19970513 (60)
DT Utility
FS APPLICATION
LREP Mackiewicz & Norris LLP, One Liberty Place - 46th Floor, Philadelphia, PA, 19103
CLMN Number of Claims: 38
ECL Exemplary Claim: 1
DRWN 1 Drawing Page(s)
LN.CNT 4899
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention is directed to a solid porous matrix comprising a surfactant in combination with a bioactive agent. The solid porous matrix may be **prepared** by combining a surfactant and a therapeutic, together with a solvent, to form an emulsion containing random aggregates of the surfactant and the therapeutic, and **processing** the emulsion by controlled drying, or controlled agitation and controlled drying to form the solid porous matrix.

L18 ANSWER 24 OF 36 USPATFULL
AN 2001:131288 USPATFULL
TI Method of treatment for uterine leiomyoma
IN Katsuki, Yukio, Tokyo, Japan
Shimora, Minoru, Tokyo, Japan
PA Mochida Pharmaceutical Co., Ltd., Tokyo, Japan (non-U.S. corporation)
PI US 6274573 B1 20010814
WO 9920647 19990429
AI US 2000-529640 20000417 (9)
WO 1998-JP4691 19981016
20000417 PCT 371 date
20000417 PCT 102(e) date
PRAI JP 1997-285826 19971017
DT Utility
FS GRANTED
EXNAM Primary Examiner: Weber, Jon P.; Assistant Examiner: Patten, Patricia D
LREP Birch, Stewart, Kolasch & Birch, LLP
CLMN Number of Claims: 11
ECL Exemplary Claim: 1

DRWN 1 Drawing Figure(s); 1 Drawing Page(s)
LN.CNT 471
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Providing a therapeutic agent of uterine leiomyoma, containing dienogest and a solvate thereof as the effective ingredient with less adverse effects, which can be used either singly or in combination with GnRH and can be administered or pharmaceutically manufactured as oral, transdermal dosing agents or suppositories.

L18 ANSWER 25 OF 36 USPATFULL
AN 2001:90260 USPATFULL
TI Fatty acid-pharmaceutical agent conjugates
IN Webb, Nigel L., Bryn Mawr, PA, United States
Bradley, Matthews O., Laytonsville, MD, United States
Swindell, Charles S., Merion, PA, United States
Shashoua, Victor E., Brookline, MA, United States
PI US 2001002404 A1 20010531
AI US 2000-730450 A1 20001205 (9)
RLI Continuation of Ser. No. US 1996-651428, filed on 22 May 1996, ABANDONED
DT Utility
FS APPLICATION
LREP Edward R. Gates, Wolf, Greenfield & Sacks, P.C., 600 Atlantic Avenue, Boston, MA, 02210
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN 14 Drawing Page(s)
LN.CNT 2511
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides conjugates of fatty acids and pharmaceutical agents useful in treating noncentral nervous system conditions. Methods for selectively targeting pharmaceutical agents to desired tissues are provided.

L18 ANSWER 26 OF 36 USPATFULL
AN 2001:90106 USPATFULL
TI Methods for detecting lesions in dense breast tissue using LHRH antagonists
IN Garnick, Marc B., Brookline, MA, United States
PA Praecis Pharmaceuticals Incorporated (U.S. corporation)
PI US 2001002249 A1 20010531
AI US 2001-764626 A1 20010118 (9)
RLI Continuation of Ser. No. US 1998-67327, filed on 27 Apr 1998, GRANTED, Pat. No. US 6217844
DT Utility
FS APPLICATION
LREP LAHIVE & COCKFIELD, 28 STATE STREET, BOSTON, MA, 02109
CLMN Number of Claims: 31
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 687
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Improved methods for detecting lesions in dense breast tissue are disclosed. The methods of the invention generally feature administration to a subject of an **LHRH antagonist** in an amount and for a period of time sufficient to reduce the density of breast tissue prior to generating an image of the breast tissue, for example by mammography, to detect a lesion in the breast tissue. Packaged formulations for reducing breast density in a subject prior to generating an image of the subject's breast tissue, comprising an **LHRH antagonist** packaged with instructions for using the **LHRH antagonist** to reduce breast density in a subject prior to imaging the breast tissue, are also disclosed.

L18 ANSWER 27 OF 36 USPATFULL
AN 2001:55422 USPATFULL
TI Methods for detecting lesions in dense breast tissue using LHRH antagonists
IN Garnick, Marc B., Brookline, MA, United States
PA Praecis Pharmaceuticals, Inc., Cambridge, MA, United States (U.S. corporation)
PI US 6217844 B1 20010417
AI US 1998-67327 19980427 (9)
DT Utility
FS Granted
EXNAM Primary Examiner: Jones, Dameron
LREP Lahive & Cockfield, LLP, DeConti, Jr., Giulio A., Laccotripe, Maria C.
CLMN Number of Claims: 22
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 768
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Improved methods for detecting lesions in dense breast tissue are disclosed. The methods of the invention generally feature administration to a subject of an **LHRH antagonist** in an amount and for a period of time sufficient to reduce the density of breast tissue prior to generating an image of the breast tissue, for example by mammography, to detect a lesion in the breast tissue. Packaged formulations for reducing breast density in a subject prior to generating an image of the subject's breast tissue, comprising an **LHRH antagonist** packaged with instructions for using the **LHRH antagonist** to reduce breast density in a subject prior to imaging the breast tissue, are also disclosed.

L18 ANSWER 28 OF 36 USPATFULL
AN 2001:14464 USPATFULL
TI Pharmaceutical formulations for sustained drug delivery
IN Gefter, Malcolm L., Lincoln, MA, United States
Barker, Nicholas, Southborough, MA, United States
Musso, Gary, Hopkinton, MA, United States
Molineaux, Christopher J., Brookline, MA, United States
PA Praecis Pharmaceuticals, Inc., Cambridge, MA, United States (U.S. corporation)
PI US 6180608 B1 20010130
AI US 1997-988851 19971211 (8)
RLI Continuation-in-part of Ser. No. US 1996-762747, filed on 11 Dec 1996, now patented, Pat. No. US 5968895
DT Utility
FS Granted
EXNAM Primary Examiner: Cintins, Marianne M.; Assistant Examiner: Delacroix-Muirheid, C.
LREP Lahive & Cockfield, LLP, DeConti, Jr., Giulio A., Laccotripe, Maria C.
CLMN Number of Claims: 50
ECL Exemplary Claim: 1
DRWN 8 Drawing Figure(s); 5 Drawing Page(s)
LN.CNT 1333
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Sustained delivery formulations comprising a water-insoluble complex of a peptidic compound (e.g., a peptide, polypeptide, protein, peptidomimetic or the like) and a carrier macromolecule are disclosed. The formulations of the invention allow for loading of high concentrations of peptidic compound in a small volume and for delivery of a pharmaceutically active peptidic compound for prolonged periods, e.g., one month, after administration of the complex. The complexes of the invention can be milled or crushed to a fine powder. In powdered

form, the complexes form stable aqueous suspensions and dispersions, suitable for injection. In a preferred embodiment, the peptidic compound of the complex is an LHRH analogue, preferably an **LHRH antagonist**, and the carrier macromolecule is an anionic polymer, preferably carboxymethylcellulose. Methods of **making** the complexes of the invention, and methods of using LHRH-analogue-containing complexes to treat conditions treatable with an LHRH analogue, are also disclosed.

L18 ANSWER 29 OF 36 USPATFULL
AN 2000:167538 USPATFULL
TI Implants containing bioactive peptides
IN Deghenghi, Romano, Cheseaux Dessus B1, St. Cergue, Switzerland
PI US 6159490 20001212
AI US 2000-543707 20000405 (9)
RLI Continuation of Ser. No. US 1999-311744, filed on 14 May 1999, now patented, Pat. No. US 6077523 which is a division of Ser. No. US 1997-897942, filed on 21 Jul 1997, now patented, Pat. No. US 5945128
PRAI US 1996-25444P 19960904 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Azpuru, Carlos A.
LREP Pennie & Edmonds LLP
CLMN Number of Claims: 4
ECL Exemplary Claim: 1
DRWN 3 Drawing Figure(s); 3 Drawing Page(s)
LN.CNT 302
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A pharmaceutical implant for the delivery of an effective amount of a bioactive peptide or peptide analog over a period of 1 to 12 months. This implant has a diameter of about 1 to 2 mm, a length of between about 10 and 25 mm and is obtainable from a **process** which includes the steps of grinding a copolymer of lactic acid and glycolic acid having a ratio of glycolide to lactide units of from about 0 to 5:1 to a particle size of between about 50 and 150 .mu.m; **sterilizing** the ground copolymer with a dose of between about 1 and 2.5 Mrads of ionizing .gamma.-radiation; wetting the ground and **sterilized** copolymer with a **sterile** aqueous slurry of a bioactive peptide or peptide analog; aseptically blending the copolymer and the slurry to obtain a homogeneous mixture of the copolymer and between about 10 and 50% of the bioactive peptide or peptide analog; drying the mixture at reduced pressure and at temperature not exceeding 25.degree. C.; aseptically extruding the dried mixture at a temperature between about 70 and 110.degree. C.; and aseptically cutting a cylindrical rod from the extruded mixture to form the pharmaceutical implant.

L18 ANSWER 30 OF 36 USPATFULL
AN 2000:80885 USPATFULL
TI Taxanes
IN Swindell, Charles S., Merion, PA, United States
Shashoua, Victor E., Brookline, MA, United States
Bradley, Matthews O., Laytonsville, MD, United States
Webb, Nigel L., Bryn Mawr, PA, United States
PA Neuromedica, Inc., Conshohocken, PA, United States (U.S. corporation)
PI US 6080877 20000627
AI US 1997-868476 19970603 (8)
RLI Continuation of Ser. No. US 1996-651429, filed on 22 May 1996, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Trinh, Ba K.

LREP Wolf, Greenfield & Sacks, P.C.
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN 27 Drawing Figure(s); 14 Drawing Page(s)
LN.CNT 1034
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides taxanes that are conjugates of cis-docosahexaenoic acid and taxotere. The conjugates are useful in treating cancer.

L18 ANSWER 31 OF 36 USPATFULL
AN 2000:77041 USPATFULL
TI **Process** to manufacture implants containing bioactive peptides
IN Deghenghi, Romano, Cheseaux Dessus B1, St. Cergue, Switzerland
PI US 6077523 20000620
AI US 1999-311744 19990514 (9)
RLI Division of Ser. No. US 1997-897942, filed on 21 Jul 1997, now patented, Pat. No. US 5945128
PRAI US 1996-25444P 19960904 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Azpuru, Carlos A.
LREP Pennie & Edmonds LLP
CLMN Number of Claims: 15
ECL Exemplary Claim: 1
DRWN 3 Drawing Figure(s); 3 Drawing Page(s)
LN.CNT 353
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A pharmaceutical implant for the delivery of an effective amount of a bioactive peptide or peptide analog over a period of 1 to 12 months. This implant has a diameter of about 1 to 2 mm, a length of between about 10 and 25 mm and is obtainable from a **process** which includes the steps of grinding a copolymer of lactic acid and glycolic acid having a ratio of glycolide to lactide units of from about 0 to 5:1 to a particle size of between about 50 and 150 .mu.m; **sterilizing** the ground copolymer with a dose of between about 1 and 2.5 Mrads of ionizing .gamma.-radiation; wetting the ground and **sterilized** copolymer with a **sterile** aqueous slurry of a bioactive peptide or peptide analog; aseptically blending the copolymer and the slurry to obtain a homogeneous mixture of the copolymer and between about 10 and 50% of the bioactive peptide or peptide analog; drying the mixture at reduced pressure and at temperature not exceeding 25.degree. C.; aseptically extruding the dried mixture at a temperature between about 70 and 110.degree. C.; and aseptically cutting a cylindrical rod from the extruded mixture to form the pharmaceutical implant.

L18 ANSWER 32 OF 36 USPATFULL
AN 1999:128511 USPATFULL
TI Pharmaceutical formulations for sustained drug delivery
IN Gefter, Malcolm L., Lincoln, MA, United States
Barker, Nicholas, Southborough, MA, United States
Musso, Gary, Hopkinton, MA, United States
Molineaux, Christopher J., Brookline, MA, United States
PA Praecis Pharmaceuticals, Inc., Cambridge, MA, United States (U.S. corporation)
PI US 5968895 19991019
AI US 1996-762747 19961211 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Richter, Johann; Assistant Examiner: Delacroix-Muirheid, C.

LREP Lahive & Cockfield, LLP, Mandragouras, Amy E., DeConti, Giulio A.
CLMN Number of Claims: 32
ECL Exemplary Claim: 10
DRWN 2 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 775
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Sustained delivery formulations comprising a water-insoluble complex of a peptide and a carrier macromolecule are disclosed. The formulations of the invention allow for loading of high concentrations of peptide in a small volume and for delivery of a pharmaceutically active peptide for prolonged periods, e.g., one month, after administration of the complex. The complexes of the invention can be milled or crushed to a fine powder. In powdered form, the complexes form stable aqueous suspensions and dispersions, suitable for injection. In a preferred embodiment, the peptide of the complex is an LHRH analogue, preferably an **LHRH antagonist**, and the carrier macromolecule is an anionic polymer, preferably carboxymethylcellulose. Methods of **making** the complexes of the invention, and methods of using LHRH-analogue-containing complexes to treat conditions treatable with an LHRH analogue, are also disclosed.

L18 ANSWER 33 OF 36 USPATFULL
AN 1999:75671 USPATFULL
TI Taxane compounds and compositions
IN Bradley, Matthews O., Laytonville, MD, United States
Shashoua, Victor E., Brookline, MA, United States
Swindell, Charles S., Merion, PA, United States
Webb, Nigel L., Bryn Mawr, PA, United States
PA Neuromedica, Inc., Conshohocken, PA, United States (U.S. corporation)
PI US 5919815 19990706
AI US 1996-653951 19960522 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Reamer, James H.
LREP Wolf, Greenfield & Sacks, P.C.
CLMN Number of Claims: 8
ECL Exemplary Claim: 1,4
DRWN 27 Drawing Figure(s); 14 Drawing Page(s)
LN.CNT 940
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides taxanes that are conjugates of cis-docosahexaenoic acid and paclitaxel. The conjugates are useful in treating cancer.

L18 ANSWER 34 OF 36 USPATFULL
AN 1998:98932 USPATFULL
TI DHA-pharmaceutical agent conjugates of taxanes
IN Shashoua, Victor E., Brookline, MA, United States
Swindell, Charles S., Merion, PA, United States
Webb, Nigel L., Bryn Mawr, PA, United States
Bradley, Matthews O., Laytonsville, MD, United States
PA Neuromedica, Inc., Conshohocken, PA, United States (U.S. corporation)
PI US 5795909 19980818
AI US 1996-651312 19960522 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Jarvis, William R. A.
LREP Wolf, Greenfield & Sacks, P.C.
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN 27 Drawing Figure(s); 14 Drawing Page(s)
LN.CNT 2451

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides conjugates of cis-docosahexaenoic acid and taxanes useful in treating cell proliferative disorders. Conjugates of paclitaxel and docetaxel are preferred.

L18 ANSWER 35 OF 36 USPATFULL
AN 97:78416 USPATFULL
TI Products for administering an initial high dose of **Cetrorelix** and producing a combination package for use when treating diseases
IN Engel, Jurgen, Alzenau, Germany, Federal Republic of
Hilgard, Peter, Frankfurt, Germany, Federal Republic of
Reissmann, Thomas, Frankfurt, Germany, Federal Republic of
PA ASTA Medica Aktiengesellschaft, Dresden, Germany, Federal Republic of (non-U.S. corporation)
PI US 5663145 19970902
AI US 1994-354838 19941208 (8)
PRAI DE 1993-4342091 19931209
DT Utility
FS Granted
EXNAM Primary Examiner: Russel, Jeffrey E.
LREP Cushman Darby & Cushman IP Group of Pillsbury Madison & Sutro LLP
CLMN Number of Claims: 25
ECL Exemplary Claim: 7
DRWN No Drawings
LN.CNT 227
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB For application during the treatment of benign and malign tumour diseases, the product according to the invention containing the initial dose of **Cetrorelix** acetate and one or more maintenance doses of **Cetrorelix** acetate, **Cetrorelix** embonate or a slow-release form of **Cetrorelix**, is used as a combination **preparation** for treatment to be administered at specific time intervals.

L18 ANSWER 36 OF 36 USPATFULL
AN 96:103974 USPATFULL
TI Compositions and methods for the treatment of male-pattern baldness
IN Tien, Henry C., 5660 SW. 58 Pl., Miami, FL, United States 33143
PI US 5574011 19961112
AI US 1995-416190 19950404 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Reamer, James H.
LREP Gonzalez, P.A., Olga
CLMN Number of Claims: 43
ECL Exemplary Claim: 1
DRWN 1 Drawing Figure(s); 1 Drawing Page(s)
LN.CNT 2046
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides methods and compositions of LHRH analogs for the treatment of male-pattern baldness. Male-pattern baldness is treated by the administration of compositions containing LHRH analogs. The compositions may be administered by any of a variety of routes, including parenterally, (including subcutaneous, and intramuscular administration), topically, transdermally or transmucosally.

=> d clm 12 14 28 31 35

L18 ANSWER 12 OF 36 USPATFULL
CLM What is claimed is:
1. A solid porous matrix comprising a surfactant in combination with a

therapeutic.

2. A composition of claim 1 further comprising a solvent.

3. A composition of claim 2 wherein said solvent is selected from the group consisting of an organic solvent and an aqueous solvent.

4. A composition of claim 1 wherein said solid porous matrix is in a physical state selected from a dried state and a liquid state.

5. A composition of claim 4 wherein said liquid state further comprises a resuspending medium.

6. A composition of claim 5 wherein said resuspending medium is selected from the group consisting of an aqueous medium and an organic medium.

7. A composition of claim 6 wherein said aqueous medium is selected from the group consisting of water, buffer, physiological saline, and normal saline.

8. A composition of claim 1 further comprising a gas or gaseous precursor.

9. A composition of claim 1 wherein said surfactant is selected from the group consisting of a nonionic surfactant, peanut oil, canola oil, olive oil, safflower oil, corn oil, a terpene, linolene, squalene, squalamine, lauryltrimethylammonium bromide, cetyltrimethylammonium bromide, myristyltrimethylammonium bromide, alkyldimethylbenzylammonium chloride, benzyldimethyldodecylammonium bromide, benzyldimethyldodecylammonium chloride, benzyldimethyl hexadecylammonium bromide, benzyldimethyl hexadecylammonium chloride, benzyldimethyl tetradecylammonium bromide, benzyldimethyl tetradecylammonium chloride, cetyldimethylethylammonium bromide, cetyldimethylethylammonium chloride, cetylpyridinium bromide, cetylpyridinium chloride, a lipid, a protein, a polypeptide, a polysaccharide, a sugar, a polymer, and an acrylate.

10. A composition of claim 9 wherein said nonionic surfactant is selected from the group consisting of octoxynols, polyoxyethylene sorbitan monolaurate, polyoxyethylene sorbitan monopalmitate, polyoxyethylene sorbitan monostearate, polyoxyethylene sorbitan monooleate, and polyoxyethylene sorbitan trioleate, polyoxyethylene ethers, polyethylene glycol, fluorosurfactants, and Fluorads.RTM..

11. A composition of claim 9 wherein said protein is selected from the group consisting of collagen, fibrin, and albumin.

12. A composition of claim 9 wherein said polypeptide is selected from the group consisting of polyglutamic acid, polylysine, polyphosphazene, polyvinylalcohol, polyethyleneglycol, polypropyleneglycol, and a copolymer.

13. A composition of claim 9 wherein said polysaccharide is selected from the group consisting of starch, HETA-starch, alginic acid, hyaluronic acid, cellulose, and a saccharide.

14. A composition of claim 13 wherein said cellulose is methylcellulose.

15. A composition of claim 13 wherein said saccharide is dextran.

16. A composition of claim 9 wherein said sugar is selected from the group consisting of glucose and galactose.

17. A composition of claim 9 wherein said polymer is selected from the group consisting of a synthetic polymer, a natural polymer, and a semisynthetic polymer.

18. A composition of claim 17 wherein said synthetic polymer is polylactic acid.

19. A composition of claim 9 wherein said copolymer is selected from the group consisting of polylatcidecoglycolide and polyethylene-polypropyleneglycol.

20. A composition of claim 9 wherein said acrylate is methacrylate.

21. A composition of claim 20 wherein said methacrylate is methylmethacrylate.

22. A composition of claim 1 wherein said therapeutic is attached to the surface of said vesicle.

23. A composition of claim 1 wherein said therapeutic is encapsulated in said vesicle.

24. A composition of claim 1 wherein said solid porous matrix is selected from the group consisting of a lyophilized solid porous matrix, a spray-dried solid porous matrix, a ball-milled solid porous matrix, an agitated solid porous matrix, and any combination thereof.

25. A composition of claim 1 further comprising a blowing agent.

26. A composition of claim 7 wherein said gas is selected from the group consisting of a fluorine containing gas and nitrogen.

27. A composition of claim 26 wherein said fluorine containing gas is selected from the group consisting of a perfluorocarbon, a perfluoroether, and sulfur hexafluoride.

28. A composition of claim 7 wherein said gas or gaseous precursor is selected from the group consisting of fluorine, perfluoromethane, perfluoroethane, perfluoropropane, perfluorobutane, perfluoropentane, perfluorohexane, perfluoroheptane, perfluorooctane, perfluorononane, perfluorodecane, sulfur hexafluoride, perfluorobutylmethylether, perfluorotetrahydropyran, perfluoromethylpentylether, hexafluoropropylene, bromochlorofluoromethane, octafluoropropane, 1,1 dichloro, fluoro ethane, hexa fluoroethane, hexafluoro-2-butyne, perfluoropentane, perfluorobutane, octafluoro-2-butene, hexafluorobuta-1,3-diene, octafluorocyclopentene, hexafluoroacetone, isopropyl acetylene, allene, tetrafluoro allene, boron trifluoride, 1,2-butadiene, 1,3-butadiene, 1,2,3-trichloro, 2-fluoro-1,3-butadiene, 2-methyl, 1,3-butadiene, hexafluoro-1,3-butadiene, butadiene, 1-fluoro-butane, 2-methyl-butane, decafluoro butane, 1-butene, 2-butene, 2-methyl-1-butene, 3-methyl-1-butene, perfluoro-1-butene, perfluoro-2-butene, 4-phenyl-3-butene-2-one, 2-methyl-1-butene-3-yne, butyl nitrate, 1-butyne, 2-butyne, 2-chloro-1,1,1,4,4,4-hexafluoro-butyne, 3-methyl-1-butyne, perfluoro-2-butyne, 2-bromo-butyraldehyde, carbonyl sulfide, crotononitrile, cyclobutane, methyl-cyclobutane, octafluoro-cyclobutane, perfluoro-cyclobutene, 3-chloro-cyclopentene, cyclopropane, 1,2-dimethyl-cyclopropane, 1,1-dimethyl-cyclopropane, 1,2-dimethyl cyclopropane, ethyl cyclopropane, methyl cyclopropane, diacetylene, 3-ethyl-3-methyl diaziridine, 1,1,1-trifluoro-diazoethane, dimethyl amine, hexafluoro-dimethyl amine, dimethylethylamine, bis-(Dimethyl phosphine)amine, 2,3-dimethyl-2-norbornane, perfluoro-dimethylamine, dimethyloxonium chloride, 1,3-dioxolane-2-one,

4-methyl, 1,1,1,2-tetrafluoro ethane, 1,1,1-trifluoroethane, 1,1,2,2-tetrafluoroethane, 1,1,2-trichloro-1,2,2-trifluoroethane, 1,1 dichloro ethane, 1,1-dichloro-1,2,2,2-tetrafluoro ethane, 1,2-difluoro ethane, 1-chloro-1,1,2,2,2-pentafluoro ethane, 2-chloro, 1,1-difluoroethane, 1-chloro-1,1,2,2-tetrafluoro ethane, 2-chloro, 1,1-difluoro ethane, chloroethane, chloropentafluoro ethane, dichlorotrifluoroethane, fluoro-ethane, hexafluoro-ethane, nitro-pentafluoro ethane, nitroso-pentafluoro ethane, perfluoro ethane, perfluoro ethylamine, ethyl vinyl ether, 1,1-dichloro ethylene, 1,1-dichloro-1,2-difluoro ethylene, 1,2-difluoro ethylene, Methane, Methane-sulfonyl chloride-trifluoro, Methane-sulfonyl fluoride-trifluoro, Methane-(pentafluorothio)trifluoro, Methane-bromo difluoro nitroso, Methane-bromo fluoro, Methane-bromo chloro-fluoro, Methane-bromo-trifluoro, Methane-chloro difluoro nitro, Methane-chloro dinitro, Methane-chloro fluoro, Methane-chloro trifluoro, Methane-chloro-difluoro, Methane-dibromo difluoro, Methane-dichloro difluoro, Methane-dichloro-fluoro, Methane-difluoro, Methane-difluoro-iodo, Methane-disilano, Methane-fluoro, Methane-iodo-trifluoro, Methane-nitro-trifluoro, Methane-nitroso-trifluoro, Methane-tetrafluoro, Methane-trichlorofluoro, Methane-trifluoro, Methanesulfenylchloride-trifluoro, 2- Methyl butane, Methyl ether, Methyl isopropyl ether, Methyl lactate, Methyl nitrite, Methyl sulfide, Methyl vinyl ether, Neon, Neopentane, Nitrogen, Nitrous oxide, 1,2,3-Nonadecane tricarboxylic acid-2-hydroxytrimethylester, 1-Nonene-3-yne, Oxygen, 1,4-Pentadiene, n-Pentane, Pentane-perfluoro, 2-Pentanone-4-amino-4-methyl, 1-Pentene, 2-Pentene {cis}, 2-Pentene {trans}, 1-Pentene-3-bromo, 1-Pentene-perfluoro, Phthalic acid-tetrachloro, Piperidine-2,3,6-trimethyl, Propane, Propane-1,1,1,2,2,3-hexafluoro, Propane-1,2-epoxy, Propane-2,2 difluoro, Propane-2-amino, Propane-2-chloro, Propane-heptafluoro-1-nitro, Propane-heptafluoro-1-nitroso, Propane-perfluoro, Propene, Propyl-1,1,1,2,3,3-hexafluoro-2,3 dichloro, Propylene-1-chloro, Propylene-chloro-{trans}, Propylene-2-chloro, Propylene-3-fluoro, Propylene-perfluoro, Propyne, Propyne-3,3,3-trifluoro, Styrene-3-fluoro, Sulfur (di)-decafluoro(S2F10), Toluene-2,4-diamino, Trifluoroacetonitrile, Trifluoromethyl peroxide, Trifluoromethyl sulfide, Tungsten hexafluoride, Vinyl acetylene, Vinyl ether, and Xenon.

29. A composition of claim 1 wherein said therapeutic is selected from the group consisting of antineoplastic agents, blood products, biological response modifiers, antifungal agents, hormones, vitamins, peptides, enzymes, antiallergic agents, anticoagulation agents, circulatory drugs, antituberculars, antivirals, antianginals, antibiotics, antiinflammatories, antiprotozoans, antirheumatics, narcotics, cardiac glycosides, neuromuscular blockers, sedatives, anesthetics, radioactive particles, monoclonal antibodies, and genetic material.

30. A composition of claim 29 wherein said antineoplastic agent is selected from the group consisting of platinum compounds, adriamycin, mitomycin, ansamitocin, bleomycin, cytosine arabinoside, arabinosyl adenine, mercaptopolylysine, vincristine, busulfan, chlorambucil, melphalan, mercaptopurine, mitotane, procarbazine hydrochloride, dactinomycin, daunorubicin hydrochloride, doxorubicin hydrochloride, taxol, mitomycin, plicamycin, aminoglutethimide, estramustine phosphate sodium, flutamide, leuprolide acetate, megestrol acetate, tamoxifen citrate, testolactone, trilostane, amsacrine, asparaginase, etoposide, interferon, teniposide, vinblastine sulfate, vincristine sulfate, bleomycin, methotrexate, and carzelesin.

31. A composition of claim 30 wherein said platinum compounds are selected from the group consisting of spiroplatin, cisplatin, and

carboplatin.

32. A composition of claim 30 wherein melphalan is selected from the group consisting of L-sarolysin and phenylalanine mustard.

33. A composition of claim 30 wherein said interferon is selected from the group consisting of interferon .alpha.-2a and interferon .alpha.-2b.

34. A composition of claim 29 wherein said blood product is selected from the group consisting of perenteral iron, hemin, and hematoporphyrins.

35. A composition of claim 29 wherein said biological response modifier is selected from the group consisting of muramyldipeptide, muramyltripeptide, lymphokines, sub-units of bacteria, N-acetyl-muramyl-L-alanyl-D-isoglutamine, and prostaglandins.

36. A composition of claim 35 wherein said lymphokine is selected from the group consisting of bacterial endotoxins.

37. A composition of claim 36 wherein said bacterial endotoxin is selected from the group consisting of lipopolysaccharides and macrophage activation factor.

38. A composition of claim 35 wherein said bacteria are selected from the group consisting of Mycobacteria and Corynebacteria.

39. A composition of claim 29 wherein said antifungal agent is selected from the group consisting of ketoconazole, nystatin, griseofulvin, flucytosine, miconazole, amphotericin B, ricin, and b-lactam antibiotics.

40. A composition of claim 29 wherein said hormone is selected from the group consisting of growth hormone, melanocyte stimulating hormone, estradiol, beclomethasone dipropionate, betamethasone, betamethasone acetate, betamethasone sodium phosphate, vetamethasone disodium phosphate, vetamethasone sodium phosphate, cortisone acetate, dexamethasone, dexamethasone acetate, dexamethasone sodium phosphate, flunisolide, hydrocortisone, hydrocortisone acetate, hydrocortisone cypionate, hydrocortisone sodium phosphate, hydrocortisone sodium succinate, methylprednisolone, methylprednisolone acetate, methylprednisolone sodium succinate, paramethasone acetate, prednisolone, prednisolone acetate, prednisolone sodium phosphate, prednisolone tebutate, prednisone, triamcinolone, triamcinolone acetonide, triamcinolone diacetate, triamcinolone hexacetonide, fludrocortisone acetate, progesterone, testosterone, and adrenocortiotropic hormone.

41. A composition of claim 29 wherein said vitamin is selected from the group consisting of cyanocobalamin neinoic acid, retinoids, .alpha.-tocopherol, naphthoquinone, cholecalciferol, folic acid, and tetrahydrofolate.

42. A composition of claim 29 wherein said peptide is selected from the group consisting of angiostatin, manganese super oxide dismutase, tissue plasminogen activator, glutathione, insulin, dopamine, peptides with affinity for the GPIIbIIIa receptor, opiate peptides, human chorionic gonadotropin, corticotropin release factor, cholecystokinins, bradykinins, promoters of bradykinins, inhibitors of bradykinins, elastins, vasopressins, pepsins, glucagon, substance P, integrins, Angiotensin Converting Enzyme inhibitors, adrenocorticotropic hormone, oxytocin, calcitonins, IgG, IgA, IgM, ligands for Effector Cell Protease

Receptors, thrombin, streptokinase, urokinase, Protein Kinase C, interferons, colony stimulating factors, granulocyte colony stimulating factors, granulocyte-macrophage colony stimulating factors, tumor necrosis factors, nerve growth factors, platelet derived growth factors, lymphotoxin, epidermal growth factors, fibroblast growth factors, vascular endothelial cell growth factors, erythropoeitin, transforming growth factors, oncostatin M, interleukins, metalloprotein kinase ligands, and collagenases.

43. A composition of claim 42 wherein said peptides with affinity for the GPIIBIIIa receptor are selected from the group consisting of RGD, AGD, RGE, KGD, KGE, and KQAGDV.

44. A composition of claim 42 wherein said opiate peptides are selected from the group consisting of enkephalines and endorphins.

45. A composition of claim 42 wherein said ACE inhibitors are selected from the group consisting of captopril, enalapril, and lisinopril.

46. A composition of claim 42 wherein said interferons are selected from the group consisting of interferon .alpha., interferon .beta., and interferon .gamma..

47. A composition of claim 42 wherein said interleukins are selected from the group consisting of interleukin 1, interleukin 2, interleukin 3, interleukin 4, interleukin 5, interleukin 6, interleukin 7, interleukin 8, interleukin 9, interleukin 10, interleukin 11, and interleukin 12.

48. A composition of claim 29 wherein said enzyme is selected from the group consisting of alkaline phosphatase and cyclooxygenases.

49. A composition of claim 29 wherein said antiallergic agent is amelexanox.

50. A composition of claim 29 wherein said anticoagulation agent is selected from the group consisting of phenprocoumon and heparin.

51. A composition of claim 29 wherein said circulatory drug is propranolol.

52. A composition of claim 29 wherein said antitubercular is selected from the group consisting of para-aminosalicylic acid, isoniazid, capreomycin sulfate cycloserine, ethambutol hydrochloride ethionamide, pyrazinamide, rifampin, streptomycin sulfate.

53. A composition of claim 29 wherein said antiviral is selected from the group consisting of acyclovir, amantadine azidothymidine, ribavirin, vidarabine monohydrate.

54. A composition of claim 29 wherein said antianginal is selected from the group consisting of diltiazem, nifedipine, verapamil, erythritol tetranitrate, isosorbide dinitrate, nitroglycerin, and pentaerythritol tetranitrate.

55. A composition of claim 29 wherein said antibiotic is selected from the group consisting of dapsone, chloramphenicol, neomycin, cefaclor, cefadroxil, cephalexin, cephradine erythromycin, clindamycin, lincomycin, amoxicillin, ampicillin, bacampicillin, carbenicillin, dicloxacillin, cyclacillin, picloxacillin, hetacillin, methicillin, nafcillin, oxacillin, penicillin, ticarcillin, rifampin, and tetracycline.

56. A composition of claim 29 wherein said antiinflammatory is selected from the group consisting of diflunisal, ibuprofen, indomethacin, meclofenamate, mefenamic acid, naproxen, oxyphenbutazone, phenylbutazone, piroxicam, sulindac, tolmetin, aspirin, and salicylates.

57. A composition of claim 29 wherein said antiprotozoan is selected from the group consisting of chloroquine, hydroxychloroquine, metronidazole, quinine, and meglumine antimonate.

58. A composition of claim 29 wherein said antirheumatic is penicillamine.

59. A composition of claim 29 wherein said narcotic is selected from the group consisting of paregoric and opiates.

60. A composition of claim 59 wherein said opiates are selected from the group consisting of codeine, heroin, methadone, morphine, and opium.

61. A composition of claim 29 wherein said cardiac glycoside is selected from the group consisting of deslanoside, digitoxin, digoxin, digitalin, and digitalis.

62. A composition of claim 29 wherein said neuromuscular blocker is selected from the group consisting of atracurium mesylate, gallamine triethiodide, hexafluorenium bromide, metocurine iodide, pancuronium bromide, succinylcholine chloride, tubocurarine chloride, and vecuronium bromide.

63. A composition of claim 29 wherein said sedative is selected from the group consisting of amobarbital, amobarbital sodium, aprobarbital, butabarbital sodium, chloral hydrate, ethchlorvynol, ethinamate, flurazepam hydrochloride, glutethimide, methotrimeprazine hydrochloride, methyprylon, midazolam hydrochloride paraldehyde, pentobarbital, pentobarbital sodium, phenobarbital sodium, secobarbital sodium, talbutal, temazepam, and triazolam.

64. A composition of claim 29 wherein said anesthetic is selected from the group consisting of bupivacaine hydrochloride, chloroprocaine hydrochloride, etidocaine hydrochloride, lidocaine hydrochloride, mepivacaine hydrochloride, procaine hydrochloride, tetracaine hydrochloride, droperidol, etomidate, fentanyl citrate with droperidol, ketamine hydrochloride, methohexital sodium, and thiopental sodium.

65. A composition of claim 29 wherein said radioactive particle is selected from the group consisting of strontium, rhenium, yttrium, technetium, and cobalt.

66. A composition of claim 29 wherein said therapeutic is selected from the group consisting of ganciclovir, vascular endothelial growth factor, foscarnet, S-(1,3 hydroxyl-2-phosphonylmethoxypropyl)cytosine, nitric oxide synthase inhibitors, aldose reductase inhibitors, LY333531, cidofovir, vitamin E, aurintricarboxylic acid, somatuline, Trolox.TM., sorvudine, .alpha.-interferon, etofibrate, filgastrim, aminoguanidine, ticlopidine, ponalrestat, epalrestat, granulocyte macrophage colony stimulating factor, dipyridamole, aspirin, nipradilol, haloperidol, latanoprost, dipifevrin, vascular endothelial growth factor, timolol, dorzolamide, adaprolol enantiomers, bifemelane hydrochloride, apraclonidine hydrochloride, vaninolol, betaxolol, etoposide, 3-.alpha., 5-.beta.-tetrahydrocortisol, pilocarpine, bioerodible poly(ortho ester), and levobunolol.

67. A composition of claim 66 wherein said aldose reductase inhibitors are selected from the group consisting of sorbinil and tolrestat.

68. A composition of claim 1 wherein said therapeutic is selected from the group consisting of prostanoic acid, N-4 sulphanol benzyl-imidazole, imidazo pyridine, 3-(Bicyclyl methylene)oxindole, 15-deoxy spergualin, benzoylcarbinol salts, fumagillin, lecosim, bendazac, N-acyl-5-hydroxytryptamine, **cetrorelix** acetate, 17-.alpha.-acyl steroids, azaandrosterone, 5-.alpha.-reductase inhibitor, and antiestrogenics.

69. A composition of claim 68 wherein said antiestrogenic is 2-4-{1,2-diphenyl-1-butenyl}phenoxy)-N,N-dimethylethanamine.

70. A composition of claim 3 wherein said ethers are selected from the group consisting of methoxylated ethers, alkylated ethers, diether, triethers, oligo ethers, polyethers, cyclic ethers, crown ethers.

71. A composition of claim 3 wherein said alkylated alcohol is methanol.

72. A composition of claim 3 wherein said alkane is hexane.

73. A composition of claim 10 wherein said polyethylene glycol is polyethylene glycol Telomer-B.

74. A composition of claim 1 further comprising a targeting ligand.

75. A solid porous matarix comprising a solvent and a surfactant in combination with a therapeutic.

76. A solid porous matrix comprising a surfactant in combination with a therapeutic **prepared** by combining a solvent, a surfactant, and a therapeutic to form an emulsion; and **processing** said emulsion by controlled drying or controlled agitation and controlled drying, to form a solid porous matrix.

77. A solid porous matrix of claim 76 wherein said solvent is evaporated during said **processing**.

78. A method of **preparing** a solid porous matrix comprising a surfactant and a therapeutic, said method comprising: a. combining a solvent, a surfactant, and a therapeutic to form an emulsion; and b. **processing** said emulsion by controlled drying, or controlled agitation and controlled drying, to form a solid porous matrix.

79. A method of claim 78 further comprising adding said solid porous matrix to a resuspending medium.

80. A method of claim 78 or 79 further comprising introducing a gas or gaseous precursor into said solid porous matrix.

81. A method of claim 78 wherein said controlled drying is selected from the group consisting of lyophilizing, spray drying, or any combination thereof.

82. A method of claim 78 wherein said controlled agitation is selected from the group consisting of shaking, vortexing, ball milling, or any combination thereof.

83. A method of claim 79 wherein said resuspending medium is selected from the group consisting of an aqueous solution or an organic solution.

84. A method of claim 79 wherein said resuspending medium is a cryopreservation medium.

85. A method of claim 84 wherein said cryopreservation medium is selected from the group consisting of polyethylene glycol, sucrose, glucose, fructose, mannose, trebalose, glycerol, propylene glycol, and sodium chloride.

86. A method for the controlled delivery of a targeted therapeutic to a region of a patient comprising: (i) administering to the patient a composition having a solid porous matrix comprising a solvent, a surfactant, a therapeutic, and a gas or gaseous precursor, (ii) monitoring the composition using energy to determine the presence of the composition in the region; and (iii) releasing the therapeutic from the composition in the region using energy.

87. A method of claim 86 wherein the region of the patient is the eye and the therapeutic is selected from the group consisting of ganciclovir, vascular endothelial growth factor, foscarnet, S-(1,3 hydroxyl-2-phosphonylmethoxypropyl) cytosine, nitric oxide synthase inhibitors, aldose reductase inhibitors, LY333531, cidofovir, vitamin E, aurintricarboxylic acid, somatuline, Trolox, sorvudine, .alpha.-interferon, etofibrate, filgastrim, aminoguanidine, ticlopidine, ponalrestat, epalrestat, granulocyte macrophage colony stimulating factor, dipyridamole+aspirin, nipradilol, haloperidol, latanoprost, dipifevrin, vascular endothelial growth factor, timolol, dorzolamide, adaprolol enantiomers, bifemelane hydrochloride, apraclonidine hydrochloride, vaninolol, betaxolol, etoposide, 3-.alpha., 5-.beta.-tetrahydrocortisol, pilocarpine, bioerodible poly(ortho ester), and levobunolol.

88. A method of claim 86 wherein said therapeutic is dexamethasone, said surfactant is PEG Telomer B, and said solvent is methanol.

89. A method of claim 86 wherein said therapeutic is dexamethasone, said surfactant is PEG Telomer B, said solvent is methanol, and said gaseous precursor is perfluorobutane.

90. A method of claim 86 wherein said therapeutic is dexamethasone, said surfactant is a fluorosurfactant, said solvent is methanol, and said gaseous precursor is perfluorobutane.

91. A method of claim 86 wherein said therapeutic is acetominophen, said surfactant is a lipid, said solvent is methanol, and said gaseous precursor is perfluorobutane.

92. A method of claim 86 wherein said therapeutic is amphotericin, said surfactant is Zonyl surfactant, said solvent is methanol, and said gaseous precursor is perfluorobutane.

93. A method of claim 86 wherein said therapeutic is adriamycin, said surfactant is Tween, said solvent is methanol, and said gaseous precursor is perfluorobutane.

94. A method of claim 86 wherein said therapeutic is taxol, said surfactant is tyloxapol, said solvent is methanol, and said gaseous precursor is perfluorobutane.

95. A method of claim 86 wherein said therapeutic is tissue plasminogen activator, said surfactant is Tween, said solvent is water, and said gaseous precursor is perfluoropropane.

96. A method of claim 86 wherein said therapeutic is tissue plasminogen activator, said surfactant is polyvinyl pyrollidone, said solvent is water, and said gaseous precursor is perfluoropropane.

97. A method of claim 86 used to treat macular degeneration wherein said therapeutic comprises indomethacin, said surfactant comprises a lipid, said solvent is methanol, and said gaseous precursor is perfluoropentane.

98. A method of claim 86 for treating venous occlusive disease wherein said therapeutic is urokinase, said surfactant comprises phosphatidylcholine and polyethylene glycol 3000, said solvent is water, and said gas is perfluoropentane.

99. A method of claim 86 for treating diabetic retinopathy wherein said therapeutic is 3-[(3'-hydroxy-2'-tetralyl)methylen]-2-oxindole said surfactant is polyethylene glycol Telomer B, said solvent is water, and said gas is 1-nonfluorobutane.

100. A method of claim 86 useful in treating breast neoplasm wherein said therapeutic is tamoxifan citrate, said surfactant comprises 1-hydroxy-3-aminopropane-1,1-diphosphonate, polyethylene glycol 2000 and Zonyl, said solvent is saline, said gaseous precursor is perfluoropropane.

101. A method of claim 86 wherein said therapeutic comprises methylprednisolone, said surfactant is hydroxyapatite, said solvent is saline, and said gaseous precursor is perfluorobutane.

102. A method of claim 86 wherein said therapeutic comprises acyclovir, said surfactant is hydroxyapatite, said solvent is saline, and said gaseous precursor is perfluorobutane.

103. A method of claim 86 wherein said therapeutic comprises methylprednisolone, said surfactant comprises hydroxyapatite, 1-hydroxy-3-aminopropane-1,1-diphosphonate, and polyethylene glycol, said solvent is saline, and said gaseous precursor is perfluorobutane.

104. A method of claim 86 wherein said energy is ultrasound.

105. A method of claim 86 wherein said energy is applied before, during, after, or any combination thereof.

106. A method of claim 70 wherein said solvent is evaporated during said **processing**.

L18 ANSWER 14 OF 36 USPATFULL
CLM What is claimed is:
1. Pharmaceutical combined **preparation** comprising two active ingredients one of which is an LHRH analogue or a combination of LHRH analogues and the other of which is an anti-oestrogen having tissue-selective oestrogenic activity.

2. Combined **preparation** according to claim 1, characterised in that the LHRH analogue is an LHRH agonist or an **LHRH antagonist**.

3. Combined **preparation** according to claim 1 or 2, characterised in that the LERH analogue is selected from the group of compounds Leuprorelin, **Cetrorelix**, Buserelin, Antide, Ac-D-Nal-D-Cpa-D-Pal-Ser-Tyr-D-Cit-Leu-Lys(Mor)-D-Ala-NH.sub.2,

Ramorelix, Zoladex and derivatives thereof.

4. Combined **preparation** according to any one of claims 1 to 3, characterised in that the LHRH analogue or the combination of LHRH analogues is orally bioavailable.

5. Combined **preparation** according to any one of claims 1 to 4, characterised in that the LHRH analogue is a non-peptidergic LHRH agonist or antagonist.

6. Combined **preparation** according to any one of claims 1 to 5, characterised in that the anti-oestrogen is selected from the group of compounds Raloxifen, Droloxifen, Centchroman and derivatives thereof.

7. Combined **preparation** according to any one of claims 1 to 6, characterised in that the anti-oestrogen is of the Raloxifen type.

8. Combined **preparation** according to any one of claims 1 to 7, characterised in that the two active ingredients are in separate forms of administration.

9. Combined **preparation** according to any one of claims 1 to 7, characterised in that the two active ingredients are in joint forms of administration.

10. **Process** for the manufacture of a pharmaceutical combined **preparation**, characterised in that an LHRH analogue or a combination of LHRH analogues and an anti-oestrogen having tissue-selective activity are formulated with customary pharmaceutical carriers, excipients and/or additives, separately from one another or together.

11. **Process** according to claim 10, characterised in that the LHRH analogue or the combination of LHRH analogues and the anti-oestrogen having tissue-selective activity are formulated separately from one another.

12. **Process** according to claim 10, characterised in that the LHRH analogue or the combination of LHRH analogues and the anti-oestrogen having tissue-selective activity are formulated together.

13. The use of an LHRH analogue or a combination of LHRH analogues, and of an anti-oestrogen having tissue-selective oestrogenic activity, for the treatment of gynaecological disorders, especially for the treatment of endometrioses and myomas.

14. Use according to claim 13, characterised in that LHRH analogue and anti-oestrogen are administered simultaneously and/or in chronological sequence.

15. Packaging unit comprising two spatially separately packaged active ingredients, one of which is an LHRH analogue or a combination of LHRH analogues and the other of which is an anti-oestrogen having tissue-selective oestrogenic activity, and comprising as third component an information leaflet on the simultaneous and/or chronologically sequential administration of the forms of administration.

L18 ANSWER 28 OF 36 USPATFULL
CLM What is claimed is:
1. A packaged formulation for treating a subject for a condition treatable with an LHRH analogue, comprising: a solid ionic complex of an

LHRH angalogue and a carrier macromolecule packaged with instructions for fusing the complex for treating a subject having a condition treatable with an LHRH analogue, wherein the peptide content of said complex is 57% to 80% by weight.

2. The packaged formulation of claim 1, wherein the LHRH analogue has the following structure: Ac-D-Nal.sup.1, 4-Cl-D-Phe.sup.2, D-Pal.sup.3, N-Me-Tyr.sup.5, D-Asn.sup.6, Lys(iPr).sup.8, D-Ala.sup.10 -LHRH, and the carrier macromolecule is carboxymethylcellulose, or a pharmaceutically acceptable salt thereof.

3. In a syringe having a lumen, the improvement comprises, inclusion of a liquid suspension of a solid ionic complex of an LHRH analogue and a carrier macromolecule in the lumen, wherein the peptide content of said complex is 57% to 80% by weight.

4. The syringe of claim 3, wherein the LHRH analogue has the following structure: Ac-D-Nal.sup.1, 4-Cl-D-Phe.sup.2, D-Pal.sup.3, N-Me-Tyr.sup.5, D-Asn.sup.6, Lys(iPr).sup.8, D-Ala.sup.10 -LHRH, and the carrier macromolecule is carboxymethylcellulose, or a pharmaceutically acceptable salt thereof.

5. A method for treating a subject for a condition treatable with an LHRH analogue, comprising administering to the subject a pharmaceutical formulation comprising a solid ionic complex of an LHRH analogue and a carrier macromolecule, wherein the peptide content of said complex is 57% to 80% by weight.

6. The method of claim 5, wherein the complex provides sustained delivery of the LHRH analogue to a subject for at least one week after the pharmaceutical composition is administered to the subject.

7. The method of claim 5, wherein the complex provides sustained delivery of the LHRH analogue to a subject for at least two weeks after the pharmaceutical composition is administered to the subject.

8. The method of claim 5, wherein the complex provides sustained delivery of the LHRH analogue to a subject for at least three weeks after the pharmaceutical composition is administered to the subject.

9. The method of claim 5, wherein the complex provides sustained delivery of the LHRH analogue to a subject for at least four weeks after the pharmaceutical composition is administered to the subject.

10. The method of claim 5, wherein the LHRH analogue is an **LHRH antagonist**.

11. The method of claim 10, wherein the **LHRH antagonist** has the following structure: Ac-D-Nal.sup.1, 4-Cl-D-Phe.sup.2, D-Pal.sup.3, N-Me-Tyr.sup.5, D-Asn.sup.6, Lys(iPr).sup.8, D-Ala.sup.10 -LHRH.

12. The method of claim 5, wherein the carrier macromolecule is an anionic polymer.

13. The method of claim 5, wherein the carrier macromolecule is an anionic polyalcohol derivative, or fragment thereof, or a pharmaceutically acceptable salt thereof.

14. The method of claim 5, wherein the carrier macromolecule is an anionic polysaccharide derivative, or fragment thereof, or a pharmaceutically acceptable salt thereof.

15. The method of claim 5, wherein the carrier macromolecule is carboxymethylcellulose, or a pharmaceutically acceptable salt thereof.

16. The method of claim 5, wherein the carrier macromolecule is selected from the group consisting of align, alginate, anionic acetate polymers, anionic acrylic polymers, xantham gums, anionic carageenan derivatives, anionic polygalacturonic acid derivatives, sodium starch glycolate, and fragments, derivatives and pharmaceutically acceptable salts thereof.

17. The method of claim 5, wherein the pharmaceutical formulation is administered to the subject by a parenteral route.

18. The method of claim 5, wherein the pharmaceutical formulation is administered to the subject orally.

19. The method of claim 5, wherein the pharmaceutical formulation is administered by intramuscular injection or subcutaneous/intradermal injection.

20. The method of claim 5, wherein the condition treatable with an LHRH analogue is a hormone dependent cancer.

21. The method of claim 20, wherein the hormone dependent cancer is prostate cancer.

22. The method of claim 5, wherein the condition treatable with an LHRH analogue is selected from the group consisting of benign prostatic hypertrophy, precocious puberty, endometriosis and uterine fibroids.

23. The method of claim 5, wherein the LHRH analogue is administered for in vitro fertilization or contraceptive purposes.

24. A pharmaceutical composition comprising a solid ionic complex of a pharmaceutically active peptide and a carrier macromolecule, wherein the peptide content of said complex is 57% to 80% by weight.

25. A pharmaceutical composition consisting essentially of a solid ionic complex of a pharmaceutically active peptide and a carrier macromolecule, wherein the peptide content of said complex is 57% to 80% by weight.

26. The pharmaceutical composition of any one of claim 24 or 25, wherein the pharmaceutically active peptide is cationic and the carrier macromolecule is anionic.

27. The pharmaceutical composition of any one of claim 24 or 25, wherein the pharmaceutically active peptidic compound is aniotic and the currier macromolecule is cationic.

28. The pharmaceutical composition of any one of claim 24 or 25, wherein the complex provides sustained delivery of the pharmaceutically active peptide to a subject for at least one week after the pharmaceutical composition is administered to the subject.

29. The pharmaceutical composition of any one of claim 24 or 25, wherein the complex provides sustained delivery of the pharmaceutically active peptide to a subject for at least two weeks after the pharmaceutical composition is administered to the subject.

30. The pharmaceutical composition of any one of claim 24 or 25, wherein the complex provides sustained delivery of the pharmaceutically active

peptide to a subject for at least three weeks after the pharmaceutical composition is administered to the subject.

31. The pharmaceutical composition of any one of claim 24 or 25, wherein the complex provides sustained delivery of the pharmaceutically active peptide to a subject for at least four weeks after the pharmaceutical composition is administered to the subject.

32. The pharmaceutical composition of any one of claim 24 or 25, wherein the pharmaceutically active peptide is a multivalent cationic or anionic peptide.

33. The pharmaceutical composition of any one of claim 24 or 25, wherein the peptide is 5 to 20 amino acids in length.

34. The pharmaceutical composition of any one of claim 24 or 25, wherein the peptide is 1 to 15 amino acids in length.

35. The pharmaceutical composition of any one of claim 24 or 25, wherein the peptide is 8 to 12 amino acids in length.

36. The pharmaceutical composition of any one of claim 24 or 25, wherein the carrier macromolecule is an anionic polymer.

37. The pharmaceutical composition of any one of claim 24 or 25, wherein the carrier macromolecule is an anionic polyalcohol derivative, or fragment thereof.

38. The pharmaceutical composition of any one of claim 24 or 25, wherein the carrier macromolecule is an anionic polysaccharide derivative, or fragment thereof.

39. The pharmaceutical composition of any one of claim 24 or 25, wherein the carrier macromolecule is carboxymethylcellulose, or a fragment or derivative thereof.

40. The pharmaceutical composition of any one of claim 24 or 25, wherein the carrier macromolecule is selected from the group consisting of align, alginate, anionic acetate polymers, anonic acrylic polymers, xantham gums, anionic carageenan derivatives, anionic polygalacturonic acid derivatives, sodium starch glycolate, and fragments, derivatives and pharmaceutically acceptable salts thereof.

41. The pharmaceutical composition of any one of claim 24 or 25, which is a lyophilized solid.

42. The pharmaceutical composition of any one of claim 24 or 25, wherein said solid ionic complex is suspended as a liquid suspension or dispersed as a semi-solid dispersion.

43. The pharmaceutical composition of any one of claim 24 or 25, wherein said pharmaceutically active peptide is an LHRH analogue.

44. The pharmaceutical composition of claim 43 wherein the LHRH analogue is an **LHRH antagonist** comprising a peptide compound, wherein a residue of the peptide compound corresponding to the amino acid at position 6 of natural mammalian LHRH comprises a D-asparagine structure.

45. The pharmaceutical composition of claim 43 wherein the LHRH analogue is an **LHRH antagonist** comprising a peptide compound comprising a structure: A-B-C-D-E-F-G-H-I-J wherein A is pyro-Glu,

Ac-D-Nal , Ac-D-Qal, Ac-Sar, or Ac-D-Pal B is His or 4-Cl-D-Phe C is Trp, D-Pal, D-Nal, L-Nal, D-Pal(N-O), or D-Trp D is Ser E is N-Me-Ala, Tyr, N-Me-Tyr, Ser, Lys(iPr), 4-Cl-Phe, His, Asn, Met, Ala, Arg or Ile; F is D-Asn, D-Gln, or D-Thr; G is Leu or Trp; H is Lys(iPr), Gln, Met, or Arg I is Pro; and J is Gly-NH.sub.2 or D-Ala-NH.sub.2 ; or a pharmaceutically acceptable salt thereof.

46. The pharmaceutical composition of claim 43, wherein the LHRH analogue is an **LHRH antagonist** having the following structure: Ac-D-Nal.sup.1, 4-Cl-D-Phe.sup.2, D-Pal.sup.3, N-Me-Tyr.sup.5, D-Asn.sup.6, Lys(iPr).sup.8, D-Ala.sup.10 -LHRH.

47. The pharmaceutical composition of claim 43 wherein said pharmaceutically active peptide is an **LHRH antagonist** .

48. The pharmaceutical composition of claim 43, wherein the LHRH analogue is the LHRH agonist Leuprolide having the structure pGlu-His-Trp-Ser-Tyr-D-Leu-Leu-Arg-Pro(ethylamide)-Gly.

49. The pharmaceutical composition of claim 43, wherein the LHRH analogue is the **LHRH antagonist Cetrorelix** having the structure Ac-D-Nal-4-Cl-D-Phe-D-Pal-Ser-Tyr-D-Cit-Leu-Arg-Pro-D-Ala.

50. The pharmaceutical composition of any one of claim 24 or 25, wherein said pharmaceutically active peptide is selected from the group consisting of bradykinin analogues, parathyroid hormone, adenocorticotrophic hormone, calcitonin, and vasopressin analogues.

L18 ANSWER 31 OF 36 USPATFULL

CLM What is claimed is:

1. A pharmaceutical implant for the delivery of an effective amount of a bioactive and water-soluble peptide or peptide analog over a period of 1 to 12 months, said implant having a diameter of about 1 to 2 mm and a length of between about 10 and 25 mm and being obtainable from a **process** which comprises: grinding a copolymer of lactic acid and glycolic acid having a ratio of glycolide to lactide units of from about 0 to 5:1 to a particle size of between about 50 and 150 .mu.m; wetting said ground and **sterilized** copolymer with a **sterile** aqueous slurry of a bioactive peptide or peptide analog; blending the copolymer and the slurry to obtain a homogeneous mixture of said copolymer and between about 10 and 50% of the bioactive peptide or peptide analog; drying said mixture at reduced pressure and at temperature not exceeding 25.degree. C.; extruding said dried mixture at a temperature between about 70 and 110.degree. C.; and cutting a cylindrical rod from the extruded mixture to form the pharmaceutical implant.

2. The implant of claim 1 wherein the **process** further comprises **sterilizing** said ground copolymer with a dose of between about 1 and 2.5 Mrads of ionizing .gamma.-radiation before adding the aqueous slurry thereto.

3. The implant of claim 1 wherein the **process** further comprises conducting the blending, extruding and cutting steps are conducted aseptically.

4. The implant of claim 1 wherein the **process** further comprises selecting the copolymer to be used to be one which is soluble in benzene and has an inherent viscosity of from 0.51 to 1 (1% in

benzene).

5. The implant of claim 1 wherein the amount of slurry is controlled so that the amount of water in the mixture is between about 35 and 65 ml. per 100 grams copolymer.

6. The implant of claim 1 wherein the amount of slurry is controlled so that the amount of bioactive peptide or peptide analog in the rods is between about 10 to 50 percent by weight.

7. The implant of claim 1 wherein the ratio of glycolide to lactide units in the copolymer ranges from about 0.5:1 to 3:1.

8. The implant of claim 1 wherein the bioactive peptide or peptide analog is an agonist or antagonist of LHRH, GnRH, growth hormone releasing hormone, growth hormone releasing peptide, angiotensin, bombesin, bradykin, cholecystokinin, enkephalin, neurokinin, tachykinin or substance P.

9. The implant of claim 1 wherein the bioactive peptide or peptide analog is a renin inhibitor, a protease inhibitor, a metallopeptidase inhibitor, enkephalinase and atrial or brain natriuretic factor degrading enzyme inhibitor.

10. The implant of claim 1 wherein the bioactive peptide or peptide analog is a pharmaceutically acceptable salt of leuprolide, goserelin, triptorelin, buserelin, avorelin, deslorelin, histrelin, **cetrorelix**, teverelix, ramorelix, antide, nictide, azaline B, azaline C or ganirelix.

11. The implant of claim 1 contained in an implanter device with a retractable needle and suitable for subcutaneous injection under the skin of a mammal.

12. A pharmaceutical implant for the delivery of an effective amount of a bioactive and water-soluble peptide or peptide analog over a period of 1 to 12 months, said implant having a diameter of about 1 to 2 mm and a length of between about 10 and 25 mm and the bioactive peptide or peptide analog is present in the rods in an amount of between about 10 to 50 percent by weight.

13. The implant of claim 12 wherein the bioactive peptide or peptide analog is an agonist or antagonist of LHRH, GnRH, growth hormone releasing hormone, growth hormone releasing peptide, angiotensin, bombesin, bradykin, cholecystokinin, enkephalin, neurokinin, tachykinin or substance P.

14. The implant of claim 12 wherein the bioactive peptide or peptide analog is a renin inhibitor, a protease inhibitor, a metallopeptidase inhibitor, enkephalinase and atrial or brain natriuretic factor degrading enzyme inhibitor.

15. The implant of claim 12 wherein the bioactive peptide or peptide analog is a pharmaceutically acceptable salt of leuprolide, goserelin, triptorelin, buserelin, avorelin, deslorelin, histrelin, **cetrorelix**, teverelix, ramorelix, antide, nictide, azaline B, azaline C or ganirelix.

L18 ANSWER 35 OF 36 USPATFULL
CLM What is claimed is:
1. A kit comprising (a) an initial dose of an **LHRH**

antagonist suitable for treatment of hormone-dependent conditions, and (b) at least one maintenance dose of the **LHRH antagonist**, in an amount which is insufficient for treating the hormone-dependent conditions when administered alone.

2. The kit of claim 1, wherein the **LHRH antagonist** of (b) is in a slow-releasing formulation.

3. The kit of claim 1, wherein the **LHRH antagonist** is **Cetrorelix**.

4. The kit of claim 3, wherein the initial dose of **Cetrorelix** is between about 1 and about 60 mg.

5. The kit of claim 3, wherein the maintenance dose of **Cetrorelix** is between about 0.1 and about 60 mg.

6. The kit of claim 3, wherein the maintenance dose of **Cetrorelix** consists of a slow-releasing formulation.

7. A method of treating a hormone-dependent condition which comprises the steps of (a) administering an initial dose of an **LHRH antagonist** to a person having a hormone-dependent condition, and (b) then administering to that person a maintenance dose of an **LHRH antagonist** in an amount which is insufficient for treating the hormone-dependent conditions when administered alone.

8. The method of claim 7, wherein the maintenance dose of the **LHRH antagonist** is a slow-releasing formulation.

9. The method of claim 7, wherein the **LHRH antagonist** is **Cetrorelix**.

10. The method of claim 7, wherein **Cetrorelix** of the maintenance dose consists of a slow-releasing formulation.

11. The method of claim 9, wherein the initial dose of **Cetrorelix** is between about 1 and about 60 mg, and the maintenance dose of **Cetrorelix** is between about 0.1 and about 30 mg.

12. The method of claim 11, wherein the **Cetrorelix** of the maintenance dose consists of a slow-releasing formulation.

13. The method of claim 7, wherein the hormone-dependent condition is prostate cancer.

14. The method of claim 7, wherein the hormone-dependent condition is endometrial hyperplasia.

15. The method of claim 7, wherein the hormone-dependent condition is benign prostate hypertrophy.

16. The method of claim 7, wherein the hormone-dependent condition is mammary carcinoma.

17. The method of claim 7, wherein the hormone-dependent condition is ovarian carcinoma.

18. The method of claim 7, wherein the hormone-dependent condition is uterine fibroma.

19. The method of claim 7, wherein the hormone-dependent condition is pubertas praecox.

20. The method of claim 7, wherein the hormone-dependent condition is pituitary adenomas.

21. A method for decreasing male fertility comprising the steps of (a) administering to a male an initial dose of an **LHRH antagonist**, and (b) then administering to that male a maintenance dose of an **LHRH antagonist** in an amount which is insufficient for decreasing male fertility when administered alone.

22. The method of claim 21, wherein the **LHRH antagonist** is **Cetrorelix**.

23. The method of claim 21, wherein the **Cetrorelix** of the maintenance dose consists of a slow-releasing formulation.

24. The method of claim 22, wherein the initial dose of **Cetrorelix** is between about 1 and 60 mg, and the maintenance dose of **Cetrorelix** is between about 0.1 and 30 mg.

25. The method of claim 24, wherein the **Cetrorelix** of the maintenance dose comprises **Cetrorelix** pamoate or **Cetrorelix** acetate in a slow-releasing form.

```
=> d his

     (FILE 'HOME' ENTERED AT 10:19:36 ON 03 JUL 2002)

     FILE 'BIOSIS, MEDLINE, AGRICOLA, EMBASE, CABA, WPIDS, JAPIO, BIOTECHDS,
     LIFESCI, CAPLUS, USPATFULL, USPAT2' ENTERED AT 10:19:54 ON 03 JUL 2002
                E ENGEL JURGEN/AU
L1           237 S E3
                E ENGEL J/AU
L2          2211 S E3
                E WICHERT BURKHARD/AU
L3            13 S E3-E4
                E WICHERT B/AU
L4            49 S E3-E5
                E SAUERBIER DIETER/AU
L5            48 S E1-E3
                E REISSMANN THOMAS/AU
L6            65 S E1-E4
                E REISSMANN T/AU
L7           105 S E3
L8          2624 S L1-L7
L9           146 S L8 AND CETRORELIX
L10           66 DUP REM L9 (80 DUPLICATES REMOVED)
L11            4 S L10 AND STERIL?
L12            4 S L10 AND LYOPHIL?
L13           10 S L10 AND (PREPAR? OR MAKIN?)
L14         4916 S CETRORELIX OR LHRH ANTAGONIST OR GNRH ANTAGONIST
L15          875 S L14 AND (PREPAR? OR MAKING OR PROCESS?)
L16          160 S L15 AND STERIL?
L17          158 DUP REM L16 (2 DUPLICATES REMOVED)
L18           36 S L17 AND CETRORELIX

=> s l17 and acetic acid
```

```
   8 FILES SEARCHED...
L19         99 L17 AND ACETIC ACID

=> s l19 and cetrorelix
L20         12 L19 AND CETRORELIX

=> d bib ab 1-12

L20  ANSWER 1 OF 12  WPIDS (C) 2002 THOMSON DERWENT
AN   1994-265229 [33]   WPIDS
DNC  C1994-121294
TI   Freeze-dried peptide compsns. - prepd. by freeze drying soln. of peptide
     in aq. acetic acid.
DC   B04
IN   ENGEL, J; REISSMANN, T; SAUERBIER, D; WICHERT, B; BURKHARD, W; JUERGEN, E
PA   (ASTA) ASTA MEDICA AG
CYC  32
PI   EP 611572     A2 19940824 (199433)* DE    5p
         R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
     DE 4305225    A1 19940825 (199433)        5p
     AU 9455235    A  19940825 (199436)
     NO 9400564    A  19940822 (199436)
     CA 2115943    A  19940820 (199439)
     CZ 9400312    A3 19940914 (199439)
     BR 9400617    A  19940927 (199440)
     SK 9400195    A3 19940907 (199440)
     FI 9400779    A  19940820 (199441)
     JP 06271476   A  19940927 (199443)        5p
     ZA 9401136    A  19941026 (199444)       12p
     HU 67117      T  19950228 (199514)
     EP 611572     A3 19950111 (199538)
     AU 671881     B  19960912 (199644)
     CN 1112019    A  19951122 (199737)
     SG 46632      A1 19980220 (199822)
     BR 1101004    A3 19980512 (199828)
     CZ 284314     B6 19981014 (199847)
     NZ 314707     A  19990225 (199914)
     CZ 285768     B6 19991117 (200002)
     EP 611572     B1 20000607 (200032)  DE
         R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
     DE 59409389   G  20000713 (200037)
     HU 218281     B  20000728 (200045)
     RU 2145234    C1 20000210 (200048)
     ES 2148247    T3 20001016 (200058)
     TW 387812     A  20000421 (200061)
ADT  EP 611572 A2 EP 1994-101672 19940204; DE 4305225 A1 DE 1993-4305225
     19930219; AU 9455235 A AU 1994-55235 19940217; NO 9400564 A NO 1994-564
     19940218; CA 2115943 A CA 1994-2115943 19940218; CZ 9400312 A3 CZ 1994-312
     19940214; BR 9400617 A BR 1994-617 19940218; SK 9400195 A3 SK 1994-195
     19940218; FI 9400779 A FI 1994-779 19940218; JP 06271476 A JP 1994-20532
     19940217; ZA 9401136 A ZA 1994-1136 19940218; HU 67117 T HU 1994-481
     19940218; EP 611572 A3 EP 1994-101672 19940204; AU 671881 B AU 1994-55235
     19940217; CN 1112019 A CN 1994-101378 19940218; SG 46632 A1 SG 1996-6874
     19940204; BR 1101004 A3 BR 1997-1101004 19970514; CZ 284314 B6 CZ 1994-312
     19940214; NZ 314707 A Div ex NZ 1994-250906 19940217, NZ 1994-314707
     19940217; CZ 285768 B6 CZ 1998-974 19940214; EP 611572 B1 EP 1994-101672
     19940204, Related to EP 1999-102340 19940204; DE 59409389 G DE 1994-509389
     19940204, EP 1994-101672 19940204; HU 218281 B HU 1994-481 19940218; RU
     2145234 C1 RU 1994-5001 19940218; ES 2148247 T3 EP 1994-101672 19940204;
     TW 387812 A TW 1994-100769 19940131
FDT  AU 671881 B Previous Publ. AU 9455235; CZ 284314 B6 Previous Publ. CZ
     9400312; NZ 314707 A Div ex NZ 250906; CZ 285768 B6 Previous Publ. CZ
```

9800974; EP 611572 B1 Related to EP 947200; DE 59409389 G Based on EP 611572; HU 218281 B Previous Publ. HU 67117; ES 2148247 T3 Based on EP 611572
PRAI DE 1993-4305225 19930219
AB EP 611572 A UPAB: 19991110
Freeze-dried compsns. comprising a peptide of 3-15 amino acid units and opt. one or more matrix materials are characterised in that 1 pt. wt. of the peptide is dissolved in 100-10,000 pts. wt. of **acetic acid** and then transferred to water and the resulting soln. is freeze dried.
USE/ADVANTAGE - The compsns. esp. contain **cetrorelix** (EP 299402), which is used in the treatment of female infertility (for controlling ovulation prior to isolating egg cells for in-vitro fertilisation) and for gonad protection in male patients (e.g. undergoing ratio- or chemotherapy). The aq. **acetic acid** soln. can be **sterilised** by filtration without gelation or hydrolysis of the peptide.
Dwg.0/0

L20 ANSWER 2 OF 12 USPATFULL
AN 2002:72856 USPATFULL
TI Pharmaceutical administration form for peptides, **process** for its **preparation**, and use
IN Bauer, Horst, Hersbruck, GERMANY, FEDERAL REPUBLIC OF
Damm, Michael, Rodermark, GERMANY, FEDERAL REPUBLIC OF
Sarlikiotis, Werner, Peania, GREECE
PI US 2002039996 A1 20020404
AI US 2001-861009 A1 20010518 (9)
PRAI DE 2000-10024451 20000518
DT Utility
FS APPLICATION
LREP GABGRIEL P. KATONA L.L.P., 14th Floor, 708 Third Avenue, New York, NY, 10017
CLMN Number of Claims: 17
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 571
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to pharmaceutical administration forms suitable for parenteral administration, which contains [sic] peptides prone to aggregation in the form of their acetate, gluconate, glucuronate, lactate, citrate, ascorbate, benzoate or phosphate salts in dissolved or dispersed form and additionally comprises [sic] one of the acids mentioned as free acid.

L20 ANSWER 3 OF 12 USPATFULL
AN 2002:17328 USPATFULL
TI Dha-pharmaceutical agent conjugates of taxanes
IN Shashoua, Victor, Brookline, MA, UNITED STATES
Swindell, Charles, Merion, PA, UNITED STATES
Webb, Nigel, Bryn Mawr, PA, UNITED STATES
Bradley, Matthews, Layton, PA, UNITED STATES
PI US 2002010208 A1 20020124
AI US 2001-846838 A1 20010501 (9)
RLI Continuation of Ser. No. US 1998-135291, filed on 17 Aug 1998, ABANDONED
Continuation of Ser. No. US 1996-651312, filed on 22 May 1996, GRANTED, Pat. No. US 5795909
DT Utility
FS APPLICATION
LREP Edward R. Gates, Esq., Wolf, Greenfield & Sacks, P.C., 600 Atlantic Avenue, Boston, MA, 02210
CLMN Number of Claims: 19

ECL Exemplary Claim: 1
DRWN 14 Drawing Page(s)
LN.CNT 2437
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides conjugates of cis-docosahexaenoic acid and pharmaceutical agents useful in treating noncentral nervous system conditions. Methods for selectively targeting pharmaceutical agents to desired tissues are provided.

L20 ANSWER 4 OF 12 USPATFULL
AN 2002:14003 USPATFULL
TI Thienopyrimidine compounds, their production and use
IN Furuya, Shuichi, Tsukuba, JAPAN
Suzuki, Nobuhiro, Tsukuba, JAPAN
Choh, Nobuo, Tsukuba, JAPAN
Nara, Yoshi, Suita, JAPAN
PA Takeda Chemical Industries, Ltd., Osaka, JAPAN (non-U.S. corporation)
PI US 6340686 B1 20020122
AI US 2000-571215 20000516 (9)
RLI Continuation of Ser. No. US 530495
PRAI JP 1999-79371 19990324
JP 2000-18019 20000125
DT Utility
FS GRANTED
EXNAM Primary Examiner: Ford, John M.
LREP Chao, Mark, Ramesh, Elaine M.
CLMN Number of Claims: 24
ECL Exemplary Claim: 1
DRWN 1 Drawing Figure(s); 1 Drawing Page(s)
LN.CNT 1944
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A compound of the formula: ##STR1##

wherein R.sup.1 and R.sup.2 each is hydrogen, hydroxy, C.sub.1-4 alkoxy, C.sub.1-4 alkoxy-carbonyl or C.sub.1-4 alkyl which may be substituted; R.sup.3 is hydrogen, halogen, hydroxy or C.sub.1-4 alkoxy which may be substituted; or adjacent two R.sup.3 may form C.sub.1-4 alkylenedioxy; R.sup.4 is hydrogen or C.sub.1-4 alkyl; R.sup.6 is C.sub.1-4 alkyl which may be substituted or a group of the formula: ##STR2##

wherein R.sup.5 is hydrogen or R.sup.4 and R.sup.5 may form heterocycle; and n is 0-5, or a salt thereof, has an excellent GnRH-antagonizing activity, and is useful for preventing or treating sex hormone-dependent diseases.

L20 ANSWER 5 OF 12 USPATFULL
AN 2001:168259 USPATFULL
TI Thienopyrimidine compounds, their production and use
IN Furuya, Shuichi, Ibaraki, Japan
Suzuki, Nobuhiro, Ibaraki, Japan
Choh, Nobuo, Ibaraki, Japan
Nara, Yoshi, Osaka, Japan
PA Takeda Chemical Industries, Ltd., Osaka, Japan (non-U.S. corporation)
PI US 6297379 B1 20011002
WO 2000056739 20000928
AI US 2000-530495 20000426 (9)
WO 2000-JP1777 20000323
20000426 PCT 371 date
20000426 PCT 102(e) date
PRAI JP 1999-79371 19990324
DT Utility
FS GRANTED

EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: Rao, Deepak R.
LREP Riesen, Philippe Y., Chao, Mark
CLMN Number of Claims: 1
ECL Exemplary Claim: 1
DRWN 1 Drawing Figure(s); 1 Drawing Page(s)
LN.CNT 1679
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB ##STR1##

A compound of formula (I) wherein R.sup.1 and R.sup.2 each is hydrogen, hydroxy, C.sub.1-4 alkoxy, C.sub.1-4 alkoxy-carbonyl or C.sub.1-4 alkyl which may be substituted; R.sup.3 is hydrogen, halogen, hydroxy or C.sub.1-4 alkoxy which may be substituted; or adjacent two R.sup.3 may form C.sub.1-4 alkylenedioxy; R.sup.4 is hydrogen or C.sub.1-4 alkyl; R.sup.6 is C.sub.1-4 alkyl which may be substituted or a group of the formula (A) wherein R.sup.5 is hydrogen of R.sup.4 and R.sup.5 may form heterocycle; and n is 0-5, or a salt thereof, has an excellent GnRH-antagonizing activity, and is useful for preventing or treating sex hormone-dependent diseases.

L20 ANSWER 6 OF 12 USPATFULL
AN 2001:131288 USPATFULL
TI Method of treatment for uterine leiomyoma
IN Katsuki, Yukio, Tokyo, Japan
Shimora, Minoru, Tokyo, Japan
PA Mochida Pharmaceutical Co., Ltd., Tokyo, Japan (non-U.S. corporation)
PI US 6274573 B1 20010814
WO 9920647 19990429
AI US 2000-529640 20000417 (9)
WO 1998-JP4691 19981016
20000417 PCT 371 date
20000417 PCT 102(e) date
PRAI JP 1997-285826 19971017
DT Utility
FS GRANTED
EXNAM Primary Examiner: Weber, Jon P.; Assistant Examiner: Patten, Patricia D
LREP Birch, Stewart, Kolasch & Birch, LLP
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN 1 Drawing Figure(s); 1 Drawing Page(s)
LN.CNT 471
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Providing a therapeutic agent of uterine leiomyoma, containing dienogest and a solvate thereof as the effective ingredient with less adverse effects, which can be used either singly or in combination with GnRH and can be administered or pharmaceutically manufactured as oral, transdermal dosing agents or suppositories.

L20 ANSWER 7 OF 12 USPATFULL
AN 2001:90260 USPATFULL
TI Fatty acid-pharmaceutical agent conjugates
IN Webb, Nigel L., Bryn Mawr, PA, United States
Bradley, Matthews O., Laytonsville, MD, United States
Swindell, Charles S., Merion, PA, United States
Shashoua, Victor E., Brookline, MA, United States
PI US 2001002404 A1 20010531
AI US 2000-730450 A1 20001205 (9)
RLI Continuation of Ser. No. US 1996-651428, filed on 22 May 1996, ABANDONED
DT Utility
FS APPLICATION
LREP Edward R. Gates, Wolf, Greenfield & Sacks, P.C., 600 Atlantic Avenue, Boston, MA, 02210

CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN 14 Drawing Page(s)
LN.CNT 2511
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides conjugates of fatty acids and pharmaceutical agents useful in treating noncentral nervous system conditions. Methods for selectively targeting pharmaceutical agents to desired tissues are provided.

L20 ANSWER 8 OF 12 USPATFULL
AN 2000:80885 USPATFULL
TI Taxanes
IN Swindell, Charles S., Merion, PA, United States
Shashoua, Victor E., Brookline, MA, United States
Bradley, Matthews O., Laytonsville, MD, United States
Webb, Nigel L., Bryn Mawr, PA, United States
PA Neuromedica, Inc., Conshohocken, PA, United States (U.S. corporation)
PI US 6080877 20000627
AI US 1997-868476 19970603 (8)
RLI Continuation of Ser. No. US 1996-651429, filed on 22 May 1996, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Trinh, Ba K.
LREP Wolf, Greenfield & Sacks, P.C.
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN 27 Drawing Figure(s); 14 Drawing Page(s)
LN.CNT 1034
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides taxanes that are conjugates of cis-docosahexaenoic acid and taxotere. The conjugates are useful in treating cancer.

L20 ANSWER 9 OF 12 USPATFULL
AN 1999:75671 USPATFULL
TI Taxane compounds and compositions
IN Bradley, Matthews O., Laytonville, MD, United States
Shashoua, Victor E., Brookline, MA, United States
Swindell, Charles S., Merion, PA, United States
Webb, Nigel L., Bryn Mawr, PA, United States
PA Neuromedica, Inc., Conshohocken, PA, United States (U.S. corporation)
PI US 5919815 19990706
AI US 1996-653951 19960522 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Reamer, James H.
LREP Wolf, Greenfield & Sacks, P.C.
CLMN Number of Claims: 8
ECL Exemplary Claim: 1,4
DRWN 27 Drawing Figure(s); 14 Drawing Page(s)
LN.CNT 940
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides taxanes that are conjugates of cis-docosahexaenoic acid and paclitaxel. The conjugates are useful in treating cancer.

L20 ANSWER 10 OF 12 USPATFULL
AN 1998:98932 USPATFULL
TI DHA-pharmaceutical agent conjugates of taxanes
IN Shashoua, Victor E., Brookline, MA, United States

Swindell, Charles S., Merion, PA, United States
Webb, Nigel L., Bryn Mawr, PA, United States
Bradley, Matthews O., Laytonsville, MD, United States
PA Neuromedica, Inc., Conshohocken, PA, United States (U.S. corporation)
PI US 5795909 19980818
AI US 1996-651312 19960522 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Jarvis, William R. A.
LREP Wolf, Greenfield & Sacks, P.C.
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN 27 Drawing Figure(s); 14 Drawing Page(s)
LN.CNT 2451
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides conjugates of cis-docosahexaenoic acid and taxanes useful in treating cell proliferative disorders. Conjugates of paclitaxel and docetaxel are preferred.

L20 ANSWER 11 OF 12 USPATFULL
AN 97:78416 USPATFULL
TI Products for administering an initial high dose of **Cetrorelix** and producing a combination package for use when treating diseases
IN Engel, Jurgen, Alzenau, Germany, Federal Republic of
Hilgard, Peter, Frankfurt, Germany, Federal Republic of
Reissmann, Thomas, Frankfurt, Germany, Federal Republic of
PA ASTA Medica Aktiengesellschaft, Dresden, Germany, Federal Republic of (non-U.S. corporation)
PI US 5663145 19970902
AI US 1994-354838 19941208 (8)
PRAI DE 1993-4342091 19931209
DT Utility
FS Granted
EXNAM Primary Examiner: Russel, Jeffrey E.
LREP Cushman Darby & Cushman IP Group of Pillsbury Madison & Sutro LLP
CLMN Number of Claims: 25
ECL Exemplary Claim: 7
DRWN No Drawings
LN.CNT 227
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB For application during the treatment of benign and malign tumour diseases, the product according to the invention containing the initial dose of **Cetrorelix** acetate and one or more maintenance doses of **Cetrorelix** acetate, **Cetrorelix** embonate or a slow-release form of **Cetrorelix**, is used as a combination **preparation** for treatment to be administered at specific time intervals.

L20 ANSWER 12 OF 12 USPATFULL
AN 96:103974 USPATFULL
TI Compositions and methods for the treatment of male-pattern baldness
IN Tien, Henry C., 5660 SW. 58 Pl., Miami, FL, United States 33143
PI US 5574011 19961112
AI US 1995-416190 19950404 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Reamer, James H.
LREP Gonzalez, P.A., Olga
CLMN Number of Claims: 43
ECL Exemplary Claim: 1
DRWN 1 Drawing Figure(s); 1 Drawing Page(s)
LN.CNT 2046

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides methods and compositions of LHRH analogs for the treatment of male-pattern baldness. Male-pattern baldness is treated by the administration of compositions containing LHRH analogs. The compositions may be administered by any of a variety of routes, including parenterally, (including subcutaneous, and intramuscular administration), topically, transdermally or transmucosally.